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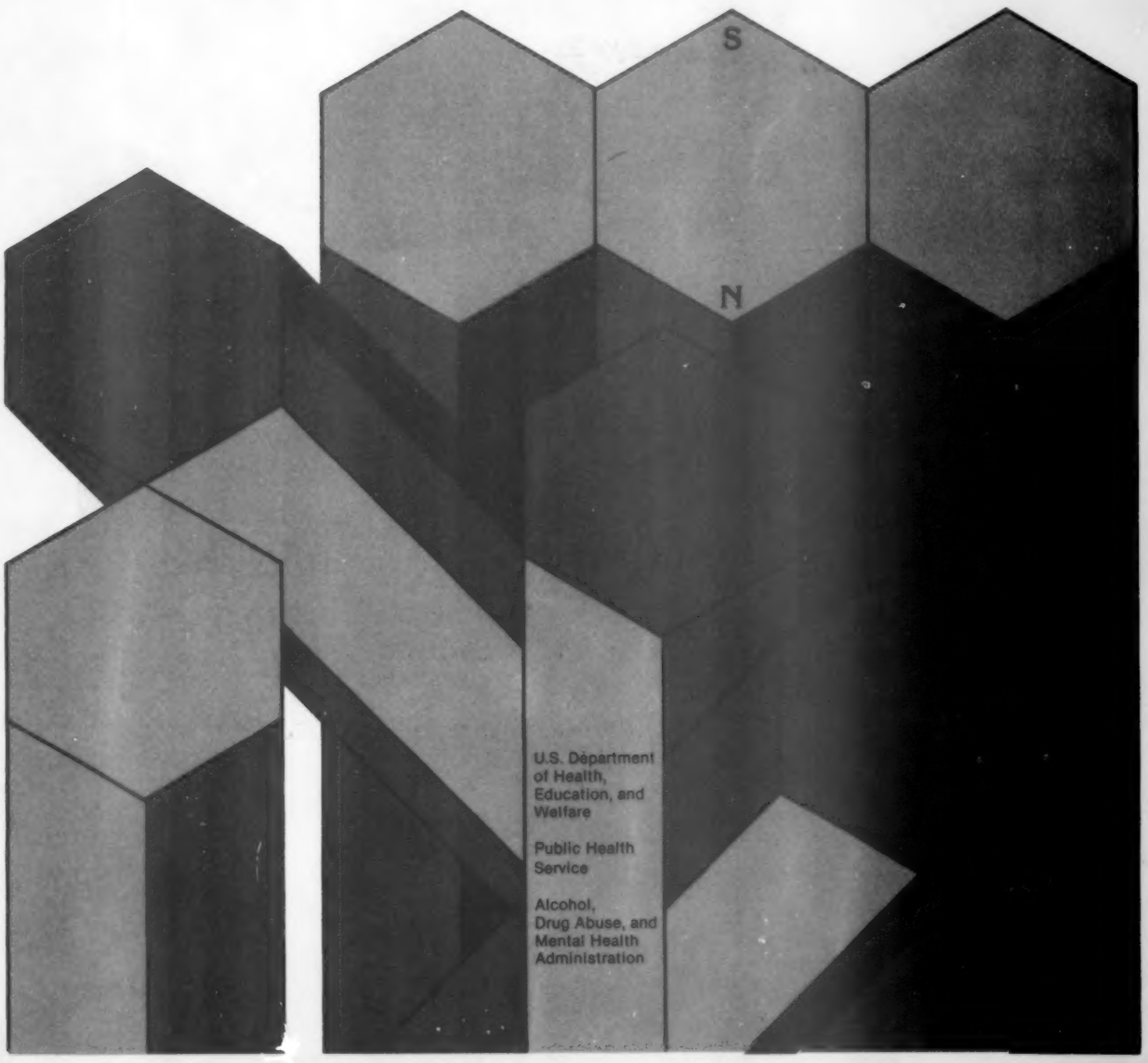

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Carrie Lee Rothgeb, *Editor*
Bette L. Shannon, *Managing Editor*

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

002786 Brown, Walter Armin; Corriveau, Donald P.; Ebert, Michael H. Neuroendocrine Research Laboratory, V.A. Hospital, Davis Park, Providence, RI **Acute psychologic and neuroendocrine effects of dextroamphetamine and methylphenidate.** Psychopharmacology (Berlin). 58(2):189-195, 1978.

The effects of dextroamphetamine (10 or 20mg) and methylphenidate (10 or 20mg) on psychologic state and serum concentrations of growth hormone, cortisol, and amphetamine were determined in 59 young male subjects. There was considerable variance in both the endocrine and psychologic responses to these drugs. In general, the higher doses of both amphetamine and methylphenidate stimulated growth hormone release, while only dextroamphetamine stimulated cortisol release. The variance in psychologic response precluded statistically significant differences among the drug groups, but the two drugs appeared to be about equally effective in eliciting euphoria, while cortisol response correlated somewhat selectively with increases in arousal. Serum amphetamine concentration correlated only with degree of growth hormone response and degree of elation. Findings suggest that a common central mechanism underlies both the growth hormone response and euphoria elicited by these drugs, while a different mechanism underlies the cortisol and arousal responses. 20 references. (Author abstract modified)

002787 Day, Alan R.; Carney, John M.; Rosecrans, John A.; Dewey, William L.; Freer, Richard J. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Synthesis of two enzyme resistant enkephalin analogs possessing enhanced analgesic activity.** Research Communications in Chemical Pathology and Pharmacology. 20(1):59-68, 1978.

Two enzyme resistant analogs of methionine enkephalin (H-Tyr-Gly-Gly-Phe-Met-OH) were synthesized and tested for morphine like properties in the stimulated guinea pig ileum, rat tail flick, mouse tail flick and for stability in whole brain homogenates. The two analogs are: Nalpha-Methyl-Tyrosyl-Glycyl-Glycyl-Phenlalanyl-des-carboxy-Norleucine (1) and Tyrosyl-D-Alanyl-Glycyl-Phenylalanyl-des-carboxy-Norleucine (2). Both peptides were completely stable for 90 minutes when incubated with whole brain homogenate (rat) while methionine enkephalin was rapidly destroyed. In addition, each peptide was found to be more potent than methionine enkephalin in the stimulated guinea pig ileum assay and had good activity in the tail flick test when given intraventricularly in mice or via indwelling catheters into the periaqueductal gray of rats. Each of these activities were blocked by naloxone. Results also show that antinociceptive activity of these peptides was much reduced in morphine tolerant animals. 16 references. (Author abstract)

002788 Di Giulio, A. M.; Yang, H.-Y. T.; Lutold, B.; Fratta, W.; Hong, J.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Characterization of enkephalin-like material extracted from sympathetic ganglia.** Neuropharmacology (Oxford). 17(11):989-992, 1978.

Both (met5)-enkephalin (ME) and (leu5)-enkephalin (LE) were extracted from the coeliac and superior cervical ganglia of rats, guinea pigs, and rabbits, along with a variable amount of immunoreactive material (against antibodies to ME and LE). The high molecular weight (greater than 1800 daltons) immunoreactive material differed from that found in caudate nucleus, in that its immunoreactivity failed to increase after trpsinization. The ratio of ME/LE was lower in ganglia than in other tissues, and LE and ME did not appear to be present in the preganglionic axons. Severing the postganglionic nerve of the superior cervical sympathetic nerve increased the amount of immunoreactive material present in the ganglia, suggesting that ME, LE, and the enkephalin like material of ganglia are located in cell bodies that send axons outside the ganglia. Immunoreactive material was also found in the adrenal medulla, suggesting that ME and LE may be present in cells that store catecholamines. However, the storage of ME and LE in sympathetic ganglia was not affected by high doses of reserpine. 10 references. (Author abstract modified)

002789 Karobath, Manfred; Sperk, Gunther; Schonbeck, Georg. Department of Experimental Psychiatry, Psychiatrische Universitatsklinik, University of Vienna, Lazarettgasse 14, A-1090 Vienna, Austria **Evidence for an endogenous factor interfering with 3H-diazepam binding to rat brain membranes.** European Journal of Pharmacology (Amsterdam). 49(3):323-326, 1978.

An endogenous 3H-diazepam binding inhibitory factor was found in rat, mouse, bovine, and human brain, using an in vitro diazepam receptor binding assay. The compound was unevenly distributed in brain and in various peripheral organs. The partially purified compound appeared to have a low molecular weight (below 500) and was not activated by proteolytic enzymes. 9 references. (Author abstract modified)

002790 Yang, H.-Y. T.; Fratta, W.; Hong, J. S.; DiGiulio, A. M.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Detection of two endorphin-like peptides in nucleus caudatus.** Neuropharmacology (Oxford). 17(6):433-438, 1978.

Two endorphin like peptides with molecular weight larger than (met5)-enkephalin were detected in bovine caudate. The peptides were separated from (met5)-enkephalin by Biogel P-2 column chromatography and detected with a (met5)-enkephalin antibody that possesses some affinity for endorphins larger than (met5)-enkephalin but smaller than beta-endorphin. The antibody has some affinity for alpha-endorphin, but the two new peptides are not alpha, beta-endorphin or beta-lipoprotein. It is suggested that the new endorphin like peptides may function as precursors of (met5)-enkephalin in the nucleus caudatus. 14 references. (Author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

002791 Berggren, Ulf; Tallstedt, Leif; Ahlenius, Sven; Engel, Jorgen. Department of Pharmacology, University Goteborg, Goteborg, Sweden **The effect of lithium on amphetamine-induced locomotor stimulation.** Psychopharmacology (Berlin). 59(1):41-45, 1978.

The interaction of lithium with monoamine mechanisms was investigated in female albino mice of the NMRI strain. Acute lithium pretreatment partially antagonized amphetamine induced locomotor stimulation in mice. A small dose of L-dopa had no stimulant effect on locomotor activity itself but caused a dose dependent antagonism of the lithium induced suppression of the amphetamine induced locomotor stimulation. Acute lithium pretreatment had no effect on the apomorphine/clonidine induced locomotor stimulation after elimination of presynaptic activity by pretreatment with reserpine and alpha-methyl tyrosine. Results indicate that the inhibitory effect of lithium on amphetamine induced locomotor stimulation is likely to be mediated by presynaptic mechanisms (decreased release of catecholamines or

inhibition of catecholamine synthesis); lithium seems to have no effect at or beyond the catecholamine receptors. The possibility that lithium may activate neuronal systems that antagonize the catecholamine neurons cannot be ruled out. 25 references. (Author abstract modified)

002792 Bisset, G. W.; Chowdrey, H. S.; Feldberg, W. St. Thomas's Hospital Medical School, London, England **Release of vasopressin by enkephalin.** British Journal of Pharmacology (London). 62(3):370-371, 1978.

Intravenous injections of leu-enkephalin, its stable analogue (D-Ala2-D-Leu5)-enkephalin, or the C-fragment of lipoprotein (beta-endorphin) produced antidiuretic responses in the rat which were inhibited reversibly by naloxone. Injection of leu-enkephalin into the cerebral ventricles was at least 10 times more effective than intravenous injection. The antidiuretic response to (D-Ala2-D-Leu5)-enkephalin was associated with increased excretion of vasopressin in the urine. 8 references. (Author abstract modified)

002793 Borgman, R. J.; Erhardt, P. W.; Gorczynski, R. J.; Anderson, W. G. Department of Medicinal Chemistry, Arnar-Stone Laboratories, Mount Prospect, IL 60056 **(-)-(E)-2-(3,4-Dihydroxyphenyl)cyclopropylamine hydrochloride(ASL-7003): a rigid analogue of dopamine.** Journal of Pharmacy and Pharmacology (London). 30(3):193-194, 1978.

The pharmacological activity of (-)-(E)-2-(3,4-dihydroxyphenyl)cyclopropylamine hydrochloride (ASL-7003) was evaluated in the canine renal blood flow system and in the isolated canine hindlimb preparation. ASL-7003 is a conformationally restricted analogue of dopamine, designed to obtain enhanced selectivity for the dopamine receptor. Findings indicate that ASL-7003 possesses alpha-agonist properties but lacks dopaminergic activity in the canine blood flow model. The steric parameters responsible for the inactivity of the compound in the canine renal blood flow model could not be determined. ASL-7003 has not yet been evaluated in models of central dopaminergic activity, but structurally similar compounds have been found to exhibit central dopaminergic activity. 13 references.

002794 Britton, Donald R.; Fertel, Richard; Coy, David H; Kastin, Abba J. Department of Pharmacology, Ohio State University College of Medicine, Columbus, OH 43210 **Effect of enkephalin and endorphin analogs on receptors in the mouse vas deferens.** Biochemical Pharmacology (Oxford). 27(18):2275-2277, 1978.

The agonist activities of a series of endorphins in which the natural peptide sequence was altered by substitution of a single amino acid were investigated in Swiss-Webster mouse vas deferens preparations. A 10-fold increase in potency resulted from substitution of D-alanine for the glycine residue at the 2-position of the peptide sequence of alpha, beta, or gamma endorphin. The activity of the various substituted analogs of met5-enkephalin showed a 10,000-fold variation; substitution of beta-alanine at the 2-position of D-alanine at the 3-position markedly reduced the activity of the pentapeptide. D-alanine was clearly the most potent substitute for glycine at the 2-position of the enkephalins, but other substituents were also effective, especially D-leu2 and D-phe2. It is concluded that the structure dependent interaction of the endorphin molecule with its receptor is as important for its potency as its resistance to degradation. 29 references.

002795 Canon, Jeffrey G.; Houser, Vincent P. Department of Pharmacology, Schering Corporation, B-6-2, Bloomfield, NJ 07003 **Squirrel monkey active conflict test.** Physiological Psychology. 6(2):215-222, 1978.

Ten female squirrel monkeys (Saimiri sciureus) were subjected to a discrete trial conflict procedure which contained an active avoidance contingency; failure to respond during conflict trials was therefore punished. Several classes of clinically active anxiolytics, including the benzodiazepines (chlordiazepoxide and diazepam), carbamates (meprobamate), and barbiturates (sodium phenobarbital and sodium pentobarbital), were tested to determine if these drugs could alter behavior generated by this schedule. The potency and efficacy of the anxiolytic drugs compared favorably with the clinical activity of these agents in man. Several other nonanxiolytic compounds (chlorpromazine, amitriptyline, and d-amphetamine) were tested to ascertain the specificity of the conflict test in detecting the anxiolytic properties of drugs. None of these latter compounds produced an anxiolytic effect in this conflict procedure. This animal model may be a useful tool in evaluating the potency and efficacy of drugs commonly used for the treatment of anxiety in man. 16 references. (Author abstract modified)

002796 Fuller, Ray W.; Hemrick, Susan K.; Mills, Jack. Lilly Research Laboratories, Eli Lilly & Co., Indianapolis, IN 46206 **Inhibition of monoamine oxidase by N-phenacyl-cyclopropylamine.** Biochemical Pharmacology (Oxford). 27(18):2255-2261, 1978.

N-phenacyl-cyclopropylamine hydrobromide (54761) was evaluated in vivo and in vitro as a monoamine oxidase (MAO) inhibitor in rats. The compound inhibited phenylethylamine oxidation at slightly lower concentrations than were required to inhibit serotonin oxidation in vitro by rat liver, indicating a slight preference for inhibition of type-B MAO. Twelve analogues of 54761 with various substituents on the phenyl ring were also studied, but none was substantially more selective than 54761 as a type-B inhibitor and most were preferential type-A inhibitors. Although 54761 also showed a preference for type-B MAO inhibition in vivo, it was not as selective an inhibitor of type-B MAO as deprenyl. Selective type-B inhibition could be achieved in vivo 24 hours after injection of 54761 by coadministration of harmaline, which protected against inactiviation of type-A MAO by 54761 but permitted the inactivation of type-B MAO to occur. 28 references. (Author abstract modified)

002797 Messiha, F. S. Department of Pathology, Texas Tech University School of Medicine, Lubbock, TX 79409 **Antagonism of ethanol-evoked responses by amantadine: a possible clinical application.** Pharmacology Biochemistry and Behavior. 8(5):573-577, 1978.

The behavioral and biochemical effects of amantidine hydrochloride (ATD) on ethanol mediated responses were examined in mice and rats. Administration of ATD (0.5mM/kg, ip) prior to a narcotic dose of ethanol significantly decreased the central depressant action of ethanol, as measured by the duration of ethanol produced narcosis, and delayed the onset of ethanol narcosis in mice. ATD treatment prior to ethanol significantly reduced brain content of ethanol at the time of onset of ethanol narcosis as well as 30 minutes after ethanol injection, without concomitant changes in blood ethanol concentrations. ATD reduced voluntary intake of ethanol by rats given a free choice between 5% ethanol or water. Cytoplasmic liver alcohol dehydrogenase (L-ADH) and mitochondrial aldehyde dehydrogenase (L-ALDH) activities were not affected by ATD in rats maintained on water or 5% ethanol. However, nonphysiological concentrations of ATD did produce a noncompetitive inhibition of L-ADH and L-ALDH in vitro. The modification of ethanol mediated responses by ATD suggests that ATD may be clinically useful in alcohol detoxification and the management of alcohol abuse. 23 references. (Author abstract modified)

002798 Setler, Paulette E.; Sarau, Henry M.; Zirkle, Charles L.; Saunders, Harry L. Department of Biological Research, Smith Kline and French Laboratories, Philadelphia, PA 19101 **The central effects of a novel dopamine agonist.** European Journal of Pharmacology (Amsterdam). 50(4):419-430, 1978.

A new peripheral dopamine (DA) agonist, 2,3,4,5-tetrahydro-7, 8-dihydroxy-1-phenyl-1H-3-benzazepine (SK&F-38393), was tested for central activity in male rats. SK&F-38393 stimulated DA sensitive adenylate cyclase in homogenates of rat caudate and caused contralateral rotation in rats with unilateral 6-hydroxydopamine lesions of substantia nigra. The rotation was shown to be due to a direct effect on supersensitive DA receptors. Simulation of cyclic adenosine monophosphate formation and rotation were blocked by DA antagonists. In contrast to other DA agonists, SK&F-38393 did not cause stereotypy, emesis, inhibition of prolactin release, or altered DA turnover. Results suggest that the new compound may selectively stimulate supersensitive central DA receptors in vivo or may activate only a certain subclass of DA receptors, including the receptor in the renal vasculature and the adenylate cyclase coupled postsynaptic receptor in the caudate. 30 references. (Author abstract modified)

002799 Shaw, John S.; Turnbull, Michael J. Department of Biology, ICI Limited, Alderley Park, Macclesfield, Cheshire, England **In vitro profile of some opioid pentapeptide analogues.** European Journal of Pharmacology (Amsterdam). 49(3):313-317, 1978.

The opiate agonist potency of 13 synthetic enkephalin pentapeptides was compared with that of methionine-enkephalin, leucine-enkephalin, beta-endorphin, and normorphine, using the electrically stimulated guinea-pig ileum and mouse vas deferens preparations. The antagonism of these agents by naloxone was also assessed in each preparation. Results are compatible with the hypothesis that these preparations possess at least two receptor populations: gama-receptors appear to occur in both the guinea-pig ileum and the mouse deferens, whereas delta-receptors occur only in the vas deferens. If this hypothesis is correct, it follows that enkephalins act at both types of receptors, since they act as potent agonists on the guinea-pig ileum and are relatively resistant to the antagonist action of naloxone in the mouse vas deferens. 10 references. (Author abstract modified)

002800 Uzan, Andre; Le Fur, Gerard; Mitrani, Nicole; Kabouche, Marie; Donadieu, Anne-Marie. Pharmindustrie, Groupe PHARMUKA, 35, quai du Moulin de Cage, F-92231 Gennevilliers, France **Effects on striatal and mesolimbic dopamine systems of a new potential antipsychotic drug -- mezilamine -- with weak cataleptogenic properties.** Life Sciences. 23(3):261-273, 1978.

The effects of mezilamine (2-methylamino-4-N-methylpiperazino-5-methylthio-6-chloropyrimidine) on striatal and mesolimbic dopamine (DA) systems were investigated in male Sprague-Dawley rats and albino rabbits. Mezilamine inhibited DA sensitive adenylate cyclase in rat nucleus accumbens and striatum, both in vivo and in vitro. Parenteral administration of mezilamine produced a dose dependent increase in homovanillic acid in rat and rabbit brain; this increase was more marked in the limbic system than in the striatum of rabbit brain, while the reverse held true in rat brain. In rats pretreated with probenecid, mezilamine and clozapine produced greater activity in the limbic system, while the activity of chlorpromazine was more pronounced in the striatum. Mezilamine was more active than chlorpromazine in both regions. After chronic treatment (15 days), the activity of mezilamine decreased in the striatum but not in the limbic system. The low cataleptogenic activity of mezilamine could not be explained by anticholinergic or gamma-aminobutyric acid mimetic properties. 36 references. (Author abstract modified)

002801 Von Voigtlander, P. F.; Triezenberg, H. J.; Losey, E. G.; von Voigtlander, P. F. Upjohn Company, Kalamazoo, MI 49001 **Interactions between clonidine and antidepressant drugs: a method for identifying antidepressant-like agents.** Neuropharmacology (Oxford). 17(6):375-381, 1978.

Clonidine caused a moderate dose related hypothermic response in mice that was antagonized by pretreatment with multiple, but not single, doses of antidepressant standards. Alpha-adrenergic blocking agents also blocked clonidine hypothermia, but beta-adrenergic blocking agents, stimulants, barbiturates, anxiolytics, analgesics, anticholinergics, and selective 5-hydroxytryptamine uptake blockers did not display this acticity. Thus, the antagonism of clonidine hypothermia correlates well with clinical antidepressant activity, both in the spectrum of drugs displaying the activity and the characteristic delay in onset of activity. The similarity between alpha-adrenergic blocking agents and the antidepressants suggests that a common underlying mechanism of antidepressants may be an ability to alter alpha-adrenergic receptor sensitivity. In addition to blocking clonidine hypothermia, chronic imipramine antagonized the clonidine induced slowing of norepinephrine turnover. However, imipramine failed to alter the sedative, analgesic, and lethal effects of clonidine. 31 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

002802 Abdel-Latif, A. A.; Green, K.; Smith, J. P.; McPherson, J. C., Jr.; Matheny, J. L. Departments of Cell and Molecular Biology, Medical College of Georgia, Augusta, GA 30902 **Norepinephrine-stimulated breakdown of triphosphoinositide of rabbit iris smooth muscle: effects of surgical sympathetic denervation and in vivo electrical stimulation of the sympathetic nerve of the eye.** Journal of Neurochemistry (Oxford). 30(3):517-525, 1978.

Paired iris smooth muscles from rabbits were prelabelled to determine: 1) the effects of norepinephrine (NE) and other adrenergic drugs on the breakdown of triphosphoinositide (TPI) in 32P-labelled iris muscle; 2) the effects of surgical sympathetic denervation on the level and metabolism of TPI and other phospholipids in this muscle; 3) the effects of NE on TPI breakdown in 32P-labelled normal and sympathetically denervated rabbit iris muscle; 4) the effects of stimulation of the sympathetic nerve of the eye on the breakdown of TPI in 32P-labelled iris in vivo and 5) whether alpha-receptors or beta-receptors influence the TPI effect. The data suggest that TPI and its enzymes could play an important role in neurotransmission at the neuromuscular junction of smooth muscle. 59 references.

002803 Abe, Hiromi; Kato, Yuzuru; Iwasaki, Yoshiko; Chihara, Kazuo; Imura, Hiroo. Third Division, Department of Medicine, Kobe University School of Medicine, Kobe 650, Japan **Central effect of somatostatin on the secretion of growth hormone in the anesthetized rat.** Proceedings of the Society for Experimental Biology and Medicine. 159(3):346-349, 1978.

The central effect of somatostatin on plasma growth hormone (GH) secretion in urethane anesthetized male Wistar rats was examined. Injection of somatostatin into the lateral ventricle caused a significant and dose dependent increase in plasma GH. Increases in plasma GH induced by intraventricular injection of somatostatin were significantly blunted in rats with hypothalamic lesions. Somatostatin infusion into the pituitary portal vessel significantly lowered plasma GH. These results suggest that somatostatin has dual effects on GH secretion, an inhibitory effect

on the pituitary and a stimulating action somewhere in the CNS. 19 references. (Author abstract)

002804 Ader, J.-P.; Muskiet, F. A. J.; Jeuring, H. J.; Korf, J. Dept. of Biological Psychiatry, State University Hospital, Oostersingel 59, Groningen, The Netherlands **On the origin of vanillylmandelic acid and 3-methoxy-4-hydroxy-phenylglycol in the rat brain.** Journal of Neurochemistry (Oxford). 30(6):1213-1216, 1978.

The effects of electrothermic destruction and electrical stimulation of the locus coeruleus on the brain levels of vanillylmandelic acid (VMA), 3-methoxy-4-hydroxyphenylglycol (MOPEG) and noradrenaline (NA) were studied in the male albino rat. Fourteen days after destruction of the locus coeruleus, the content of NA in the hippocampus and that of MOPEG in the rest of the brain were decreased by more than 70% and 50% respectively. Stimulation of the locus coeruleus induced a decrease in hippocampal levels of NA of 38%, while MOPEG levels were found to be increased more than 3 fold. After intraventricular injection of adrenaline (A), the levels of MOPEG were substantially increased. In none of these experiments was any variation of VMA levels found. These results suggest that in the rat brain endogenous VMA is not a metabolite of either NA or A. The formation of MOPEG from A as well as from NA appears to be possible. 23 references. (Author abstract)

002805 Ahn, Ho Sam; Markman, Maynard H. Department of Biochemistry and Moelcular Pharmacology, Albert Einstein College of Medicine, Bronx, NY 10461 **Stimulation of adenylate cyclase activity in monkey anterior limbic cortex by serotonin.** Brain Research. 153(3):636-640, 1978.

The effects of serotonin on adenylate cyclase activity were studied in homogenates of the anterior limbic cortex (ALC) and frontal cortex (FC) of Cebus monkeys. Serotonin stimulated in a dose dependent manner adenylate cyclase activity in homogenates of ALC. Half maximal activation was produced by 1mcM serotonin with maximal stimulation at about 100mcM. Enzyme activity in ALC was also significantly stimulated by lysergic acid diethylamide (LSD), psilocin and capsaicin. Quipazine was without effect in monkey ALC. In marked contrast to ALC, adenylate cyclase activity of FC was not stimulated by serotonin, LSD, or capsaicin. Serotonin and LSD, at certain concentrations, inhibited the basal activity of FC enzyme. In order to further elucidate the type of receptor mediating serotoninergic stimulation of adenylate cyclase in ALC, the effects of serotonin and dopamine blocking agents were examined. Methysergide and haloperidol were equally effective in antagonizing the serotonin stimulated activity. The results, together with those of previous studies, indicate that both dopamine and serotonin sensitive adenylate cyclase systems may serve as biochemical substrates for LSD. The differential response to serotonin in FC and ALC suggests that serotonin receptors in ALC but not in FC may be coupled to adenylate cyclase. 18 references.

002806 Ahtee, Liisa; Kaakkola, Seppo. School of Pharmacy, Department of Pharmacology, University of Helsinki, Kirkkokatu 20, SF-00170 Helsinki 17, Finland **Effect of mecamylamine on the fate of dopamine in striatal and mesolimbic areas of rat brain; interaction with morphine and haloperidol.** British Journal of Pharmacology (London). 62(2):213-218, 1978.

The effects of the nicotinic cholinoceptor blocking drug, mecamylamine, alone or in combination with morphine or haloperidol, on the striatal homovanillic acid (HVA) concentration and the alpha-methyl-p-tyrosine (AMPT)-induced depletion of striatal or mesolimbic dopamine content of rat brains were investigated. Mecamylamine (2mg/kg) alone did not alter the striatal HVA concentration, but it reduced the probenecid-induced accumulation of HVA. Mecamylamine pretreatment reduced the morphine- and haloperidol-induced elevation of striatal HVA. Hexamethonium did not alter striatal HVA concentrations when given alone or in probenecid or morphine treated rats, while pempidine (8mg/kg) clearly reduced the probenecid-induced accumulation of striatal HVA. Mecamylamine (2 and 8mg/kg) slowed the rate of AMPT-induced depletion of dopamine from the striatum and mesolimbic area both in the brain of control rats and of rats treated with morphine or haloperidol. Mecamylamine slightly prolonged the cataleptic effect of morphine. The results indicate that mecamylamine inhibits the release of dopamine both from the striatal and mesolimbic dopaminergic neurons. 25 references. (Author abstract)

002807 Aizenstein, Moacyr L.; Korf, Jakob. Departmento de Fisiologia e Farmacologia, Instituto de Ciencias Biomedicas da Universidade de Sao Paulo, Brazil **Aspects of influx and efflux of homovanillic acid of rat cerebrospinal fluid.** Brain Research (Amsterdam). 149(1):129-140, 1978.

The efflux of homovanillic acid (HVA) following lumbar/cisternal or ventricular/cisternal perfusion of male Wistar rats with artificial cerebrospinal fluid was measured fluorimetrically. Intravenous administration of 20microg HVA did not substantially enhance the outflow of this acid, indicating that the HVA in the perfusate was of central origin. In the lumbar/cisternal preparation, probenecid (200mg/kg, i.p.)inhibited the efflux of a significant fraction of HVA added to the medium, at a perfusion rate of 30 or 180microl/minute; the proportion of HVA eliminated by probenecid sensitive transport was much higher at the lower rate of perfusion. Following probenecid, the increase of endogenous HVA in the ventricular/cisternal perfusate was higher at the lower rate of perfusion. The highest efflux of HVA was found in the ventricular/cisternal preparation during probenecid treatment and did not appear to be dependent upon the rate of perfusion. A maximal value of 3.5% of HVA formed in the CNS was released into the cerebrospinal fluid. 25 references. (Author abstract modified)

002808 Al Timimi, Khawla S.; Bedwani, J. R.; Stanton, A. W. B. Department of Physiology, University College, Cardiff CF1 1XL, Wales **Effects of prostaglandin E2 and a prostaglandin endoperoxide analogue on neuroeffector transmission in the rat anococcygeus muscle.** British Journal of Pharmacology (London). 63(1):167-176, 1978.

The effects of prostaglandin E2 (PGE2) and a prostaglandin endoperoxide analogue (U-46619) on the responses of male Sprague-Dawley rat anococcygeus muscle to field stimulation of the intrinsic sympathetic nerves and to exogenous noradrenaline were investigated. The effects of PGE2 on responses to stimulation of intrinsic inhibitory nerves were also studied. Results indicate that PGE2 inhibits sympathetic neurotransmission in the rat anococcygeus muscle by a prejunctional action, whereas the predominant effect of U-46619 is direct excitation of the muscle. The effect of PGE2 on inhibitory responses to field stimulation may represent an interference with inhibitory neuroeffector transmission in this tissue, or may simply be a consequence of the spasmogenic action of the prostaglandin. Results are discussed in relation to the effects of prostaglandins and prostaglandin endoperoxides on neuroeffector transmission in other sympathetically innervated tissues. 31 references. (Author abstract modified)

002809 Al-Gailany, K. A. S.; Houston, J. B.; Bridges, J. W. Department of Chemistry, University of Basrah, Iraq **The role of substrate lipophilicity in determining type 1 microsomal P450**

binding characteristics. Biochemical Pharmacology (Oxford). 27(5):783-788, 1978.

The type 1 cytochrome P450 binding of 53 aliphatic, alicyclic, and aromatic compounds to hepatic microsomes from normal hamsters and from hamsters pretreated with phenobarbitone or 3-methylcholanthrene was examined. A good correlation between binding affinity and substrate lipophilicity was observed in each series of compounds. Sterically hindered molecules tended to partially deviate from this relationship. The pronounced slopes of plots of spectral dissociation constants against the log of the partition coefficient between octanol and phosphate buffer indicate that substrate lipophilicity is the predominant requirement for type 1 binding of these compounds. Microsomes from phenobarbitone pretreated animals showed substrate binding characteristics similar to those to normal animals, while 3-methylcholanthrene pretreated animals showed a spectral shift but similar binding affinities. 28 references. (Author abstract)

002810 Annunziato, Lucio A.; Wuerthele, Suzanne M.; Moore, Kenneth E. Department of Pharmacology, Second Faculty of MEDICINE, University of Naples, Naples, Italy **Comparative effects of penfluridol on circling behavior and striatal DOPAC and serum prolactin concentrations in the rat.** European Journal of Pharmacology (Amsterdam). 50(3):187-192, 1978.

The sensitivities of the nigrostriatal and tuberoin fundibular neuronal systems to the neuroleptic penfluridol were compared. A single subcutaneous injection of 3mg/kg penfluridol in male Sprague-Dawley rats elevated serum concentrations of prolactin for more than 96 hours, but increased striatal concentrations of 3,4-dihydroxyphenylacetic acid (DOPAC) and inhibited apomorphine-induced circling behavior for less than 48 hours. The dose of penfluridol needed to elevate serum prolactin (0.1mg/kg) was less than that required to elevate striatal DOPAC concentrations (1mg/kg) or inhibit apomorphine-induced circling (3mg/kg). The penfluridol-induced increase of striatal DOPAC was more susceptible to reversal by apomorphine than was the increase of serum prolactin concentrations. Results suggest that the dopamine receptors in the pituitary, which are normally activated by dopamine released from tuberoinfundibular neurons, are more sensitive than dopamine receptors in the striatum to the blocking actions of systemically administered penfluridol. 19 references. (Author abstract modified)

002811 Antonaccio, M. J.; Kerwin, Linda; Taylor, D. G. Squibb Institute for Medical Research, Box 4000, Princeton, NJ 08540 **Effects of central GABA receptor agonism and antagonism on evoked diencephalic cardiovascular responses.** Neuropharmacology (Oxford). 17(8):597-603, 1978.

The administration of the gamma-aminobutyric acid (GABA) agonists diazepam (0.3mg/kg, intravenously) and muscimol (0.3mcg/kg, intracerebroventricularly) to chloralose anesthetized cats caused significant inhibition of the pressor responses elicited by electrical diencephalic stimulation. The inhibition was apparently the result of a reduction in centrally emanating sympathetic discharge to vasoconstrictor nerves. The GABA antagonist bicuculline (0.5mg/kg, intravenously) reversed the inhibition caused by muscimol but not by diazepam; pretreatment with bicuculline prevented the inhibition caused by diazepam, however. Muscimol caused significant and marked reductions in blood pressure and heartrate by decreasing central sympathetic nerve discharge; this action was also completely reversed by bicuculline. It is suggested that central activation of GABA receptors results in an inhibition of centrally evoked cardiovascular responses by preventing increases in sympathetic outflow. Furthermore, basal as well as evoked blood pressure, heartrate, and sympathetic nerve discharge can be reduced by small doses of the directly acting GABA receptor stimulant muscimol. 27 references. (Author abstract modified)

002812 Bacopoulos, N. G.; Bustos, G.; Redmond, D. E.; Baulu, J.; Roth, R. H. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Regional sensitivity of primate brain dopaminergic neurons to haloperidol: alterations following chronic treatment.** Brain Research (Amsterdam). 157(2):396-401, 1978.

The effects of chronic administration of haloperidol on the accumulation of dopamine (DA) metabolites and on the kinetic properties of tyrosine hydroxylase in brain regions of the primate Cercopithecus aethiops were investigated. The senstiivity of the putamen to the increase in homovanillic acid (HVA) induced by 1.0mg/kg haloperidol was attenuated by pretreatment for 19 days with 0.5mg/kg haloperidol. The sensitivity of the frontal and cingulate cortex to the HVA elevating effects of haloperidol was unchanged or enhanced in the same animals. Chronic pretreatment with haloperidol suppressed the activation of tyrosine hydroxylase in the putamen but enhanced activation in the cingulate cortex. Results indicate that chronic treatment with haloperidol produces tolerance to the drug in the putamen, while the sensitivity of dopaminergic synapses in the frontal and cingulate cortex is maintained or enhanced. 20 references.

002813 Baker, Stephen P.; Hemsworth, Brian A. Department of Pharmacology, University of Miami, School of Medicine, Miami, FL 33152 **Effect of mitochondrial lipid peroxidation on monoamine oxidase.** Biochemical Pharmacology (Oxford). 17(5):805-806, 1978.

The effect of ferrous-ion-induced mitochondrial lipid peroxidation on monoamine oxidase (MAO) activity was determined. Rat liver mitochondria were isolated, incubated, and centrifuged. Peroxidation reduced MAO activity by 28%, 23%, and 28% when tyramine, serotonin, and benzylamine were used as substrates respectively. No MAO activity was detected in the supernatant. When mercaptoethanol was present during lipid peroxidation, no significant difference was observed in the recovery of enzyme activity. Results indicate that MAO, a marker for the outer mitochondrial membrane, is relatively resistant to inactivation by ferrous-ion-induced peroxidation. 17 references.

002814 Bareggi, Silvio R.; Markey, Keith; Genovese, E. Istituto di Farmacologia, IV Cattedra, Universita di Milano, Italy **Effects of single and multiple doses of desipramine (DMI) on endogenous levels of 3-methoxy-4-hydroxyphenylglycol-sulfate (MOPEG-SO4) in rat brain.** European Journal of Pharmacology (Amsterdam). 50(4):301-306, 1978.

A single intraperitoneal injection of 10mg/kg desipramine (DMI) decreased both the brain level and the probenecid-induced accumulation rate of 3-methoxy-4-hydroxyphenylglycol-sulfate (MOPEG-SO4) in male rats. Phenoxybenzamine (20mg/kg) or chlorpromazine (10mg/kg) completely prevented the DMI-induced decrease in MOPEG-SO4 brain levels. DMI did not antagonize the increase in MOPEG-SO4 induced in the cortex/hippocampus by stimulation of the locus coeruleus. These observations indicate that the effect of DMI on MOPEG-SO4 is more likely to be due to a reduction of neuronal impulse flow mediated by a negative feedback mechanism resulting from impairment of reuptake than to a direct effect on norepinephrine catabolism. Repeated administration of DMI (10mg/kg, twice a day for 3 days) did not significantly reduce the rate of probenecid-induced accumulation of MOPEG-SO4. This development of tolerance to the metabolite decreasing effects of DMI indicates that complex adaptive changes occur in the noradrenergic system upon repeated DMI administration. 24 references. (Author abstract modified)

002815 Barkai, Amiram I. 722 W. 168th Street, New York, NY 10032 **Dopamine turnover in the intact rabbit brain: effect of pentobarbital or haloperidol.** Journal of Pharmacology and Experimental Therapeutics. 205(1):133-140, 1978.

Turnover of dopamine in the intact brain of the unanesthetized rabbit was estimated from the rate of appearance of endogenous homovanillic acid (HVA) in the cerebrospinal fluid (CSF) compartment. The rate of appearance of the dopamine metabolite was determined by isotope dilution during ventriculocisternal perfusion with artificial CSF containing [3H] HVA. Removal of HVA from the perfusate was concomitantly determined and analyzed in terms of bulk absorption, diffusion and active transport. The results of the studies of the effects of pentobarbital and haloperidol show that application of either drug results in increased HVA levels in the cerebroventricular perfusates. Haloperidol caused a 4-fold increase in the rate of appearance of HVA without affecting the processes for metabolite removal, whereas pentobarbital did not alter the rate of appearance of HVA but induced blockage of its active transport from the perfused CSF compartment. It is concluded that the perfusion method permits simultaneous estimations of the rates of appearance and disapperance of monoamine metabolites in the CSF and is therefore suitable for determining whether a change in the metabolite concentration is causally related to a change in its production or removal or both. 34 references. (Author abstract)

002816 Barker, J. L.; Smith, T. G., Jr.; Neale, J. H. Laboratory of Neurophysiology, National Institute of Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD 20014 **Multiple membrane actions of enkephalin revealed using cultured spinal neurons.** Brain Research (Amsterdam). 154(1):153-158, 1978.

Intracellular recording from mouse spinal neurons grown in tissue culture was used to investigate the membrane mechanisms underlying opiate peptide actions. Preliminary results indicate the leucine-enkephalin produces direct and indirect effects on neuronal membrane properties in ways that are operationally distinct from neurotransmitter actions on neuronal membrans. Leucine-enkephalin iontophoresed onto the cell body region rapidly and reversibly affected membrane excitability, when measured by the cell's ability to generate action potentials in response to brief depolarizing current stimuli or removal of hyperpolarizing current stimuli. In 12 of 37 neurons tested, leucine-enkephalin depressed excitability, in that spikes evoked by suprathreshold stimuli were blocked. In 4 neurons, leucine-enkephalin increased excitability, transforming the voltage responses to subthreshold, depolarizing constant current pulses into action potentials. The effect of leucine-enkephalin in 8 of 37 cells was characterized by the appearance of abrupt depolarizations of membrane potential. In addition to direct effects on membrane excitability, leucine-enkaphalin also affected excitability indirectly, by modulating responses to glutamate, glycine, and gamma-aminobutyric acid. 27 references.

002817 Behbehani, Michael M.; Pomeroy, Scott L. Department of Physiology, University of Cincinnati College of Medicine, 231 Bethesda Avenue, Cincinnati, OH 45267 **Effect of morphine injected in periaqueductal gray on the activity of single units in nucleus raphe magnus of the rat.** Brain Research (Amsterdam). 149(1):266-269, 1978.

The response of single units in the nucleus raphe magnus (NRM) to microiontophoresis or microinjection of morphine into the periaqueductal gray (PAG) was studied in male Sprague-Dawley rats. Of 37 cells in NRM tested by morphine iontophoresis, 17 cells responded; 12 cells were excited and 5 cells were inhibited. The response of these cells to morphine was reversed by naloxone. Cells responded to morphine applied in the ventral but not in the dorsal part of the PAG. In the majority of cells, the alternation in firing rate following morphine did not exceed 70-80% of the baseline firing rate. Of 32 NRM cells studied after microinjection of morphine, 11 cells were excited and 10 cells were inhibited; the effect of morphine was reversed by naloxone in 18 of these cells. Results indicate that there is a physiological projection from PAG to NRM that can be affected by morphine and that the percentage of cells in NRM that can be affected increases as the quantity of morphine injected in PAG increases (46% with iontophoresis compared to 66% with microinjection). 16 references.

002818 Benuck, M.; Marks, N. Research Institute for Neurochemistry, Rockland Research Institute, Ward's Island, NY 10035 **Inhibition of brain angiotensin-1 converting enzyme by Bothrops jararaca nonapeptide (SQ 20881) and a prolyl analog (SQ 14225).** Journal of Neurochemistry (Oxford). 30(6):1653-1655, 1978.

The inhibition of brain angiotensin-1 converting enzyme by Bothrops jararaca nonapeptide SQ 20881 and a prolyl analog (SQ 14225) were studied in male Sprague-Dawley rats. It is noted that SQ 14225 has the potential for use as an oral agent in the treatment of hypertension. Bothrops jararace peptide and its prolyl analog, SQ 14225, are considerably more potent inhibitors of the angiotens converting enzyme than either angiotensin II or saralasin. Comparison of the structure of various Bothrops jararaca peptides which inhibit the angiotensin converting enzyme indicate that C-terminal proline groups are essential. SQ 14225 is a potent inhibitor of the brain enzyme, and since it is smaller in molecular dimension than other Bothrops jararaca peptides, it might facilitate studies on the role of the renin/angiotensin system in the CNS. 17 references.

002819 Bernthal, P. J.; Koss, M. G. University of Oklahoma Health Sciences Center, College of Medicine, P. O. Box 26901, Oklahoma City, OK 73190 **Some physiologic characteristics of the electrodermal reflex in the cat.** Brain Research Bulletin. 3(5):437-441, 1978.

The amplitudes of electrodermal reflexes evoked in intact cats were examined under a variety of anesthetic conditions. Electrodermal reflexes were elicited in both decerebrate and spinal preparations, with and without anesthesia. Reflex amplitude was significantly depressed in the anesthetized preparation after decerebration or spinal transection. In contrast, spinal transection performed after decerebration in unanesthetized preparations significantly increased the amplitude of the reflex. Results support the concept of a primarily inhibitory lower brainstem system with regard to this reflex. The relative stability of the reflex amplitude in the anesthetized cat suggests that this reflex system could be useful in the analysis of effects of drugs acting on the CNS. 21 references. (Author abstract modified)

002820 Bertagni, P.; Bianchi, R.; Marcucci, F.; Mussini, E.; Garattini, S. Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea, I-62-20157 Milan, Italy **The enterohepatic circulation of oxazepam-O-glucuronide in guinea-pigs.** Journal of Pharmacy and Pharmacology (London). 30(3):185-186, 1978.

Enterohepatic circulation of oxazepam-O-glucuronide was studied in relation to the relatively low rate of disappearance of oxazepam from the blood in guinea pigs. Twelve male albino guinea pigs were injected with oxazepam-O-glucuronide at a dose corresponding to 5mg/kg of oxazepam, through a cannula placed in the duodenum through the bile duct. Following injection, the circulation of bile was interrupted in four animals, while bile circulation was normal in four guinea pigs. During the 3 hours of observation, the animals with intact biliary circu-

lation eliminated in the urine twice as much oxazepam-O-glucuronide as animals with interrupted bile circulation. The concentration of oxazepam in the blood, adipose tissue, and brains of the animals with intact biliary circulation was four to five times higher than the concentrations in animals with bile fistula. The concentrations of oxazepam-O-glucuronide in the blood of the two groups were not significantly different, perhaps as a result of high variability or a high rate of clearance. Results indicate that oxazepam-O-glucuronide excreted in the bile is rapidly absorbed through the intestine into the circulation and that the glucuronide is largely hydrolyzed to form oxazepam. 13 references.

002821 Bevan, P.; Bradshaw, C. M.; Pun, R. Y. K.; Slater, N. T.; Szabadi, E. Dept. of Psychiatry, University of Manchester, Stopford Building, Oxford Road, Manchester M13 9PT, England **Comparison of the responses of single cortical neurones to tyramine and noradrenaline: effects of desipramine.** British Journal of Pharmacology (London). 63(4):651-657, 1978.

Microelectrophoresis was used to compare the actions of tyramine and noradrenaline (NA) on single neurons in the cerebral cortex of the rat. Tyramine could both excite and depress cortical neurons. Each tyramine sensitive cell was also sensitive to NA. There was a high correlation between the directions of responses to tyramine and NA, most cells excited by tyramine being excited by NA. In the case of both excitatory and depressant responses, tyramine appeared to be less potent than NA. Tyramine evoked slower responses than NA, both the latencies to onset and the recovery times being longer for responses to tyramine than for responses to NA. When the rates of release of tyramine and NA from micropipettes were measured in vitro, no significant difference could be observed between the transport numbers of the two drugs. Desipramine could discriminate between neuronal responses to tyramine and NA: responses to tyramine were antagonized while responses to NA were either potentiated or unaffected. Results are consistent with the hypothesis that tyramine is an indirectly acting sympathomimetic amine in the brain, and desipramine acts by blocking the uptake of both tyramine and NA into presynaptic NA nerve terminals. 33 references. (Author abstract modified)

002822 Bevan, P.; Bradshaw, C. M.; Pun, R. Y. K.; Slater, N. T.; Szabadi, E. Department of Psychiatry, University of Manchester, Stopford Building, Oxford Road, Manchester, M13 9PT England **Responses of single cortical neurones to noradrenaline and dopamine.** Neuropharmacology (Oxford). 17(8):611-617, 1978.

The effects of microelectrophoretically applied noradrenaline (NA) and dopamine (DA) on single cortical neurons were investigated in male albino rats. Both excitatory and depressant responses could be evoked by both catecholamines, and every neuron studied responded in the same direction to NA and DA. NA was consistently more potent than DA in eliciting both excitatory and depressant responses. Excitatory responses to both catecholamines could be antagonized by the alpha-adrenoceptor antagonist phenoxybenzamine and by the neuroleptics haloperidol and alpha-flupenthixol. Phenoxybenzamine had a more pronounced effect on responses to NA than to DA, while the neuroleptics showed a greater antagonistic effect on responses to DA than to NA. Responses to acetylcholine were not affected by the antagonists. Beta-flupenthixol was a much less effective and less specific antagonist of responses to DA than was alpha-flupenthixol. Results suggest that excitatory response of cortical neurons to the catecholamines may be mediated by two receptor populations, alpha-adrenoceptors and excitatory DA receptors. 18 references. (Author abstract modified)

002823 Bhargava, K. P.; Jain, I. P.; Saxena, A. K.; Sinha, J. N.; Tangri, K. K. Department of Pharmacology & Therapeutics, King George's Medical College, Lucknow 226003, India **Central adrenoceptors and cholinoceptors in cardiovascular control.** British Journal of Pharmacology (London). 63(1):7-15, 1978.

The cardiovascular function of adrenoceptors and cholinoceptors in the posterior hypothalamus, lateral medullary reticular pressor area, and spirnal autonomic loci was investigated in cats anesthetized with chloralose. Effects of localized administration of adrenoceptor and cholinoceptor agonists and antagonists indicate that alpha-adrenoceptors subserve an inhibitory role and beta-adrenoceptors a facilitatory role in cardiovascular control; alpha-adrenoceptors appear to predominate at the medullary level and beta-adrenoceptors at the hypothalamic level. Nicotinic cholinoceptors at the hypothalamic, medullary, and spinal levels were facilitatory, whereas muscarinic cholinoceptors were inhibitory for cardiovascular control. Muscarinic receptors were undetectable in the posterior hypothalamus. Results suggest that the central cardiovascular effects of nicotine are due to nicotinic receptor activation and the release of central catecholamines. 35 references. (Author abstract modified)

002824 Bhattacharya, S. K.; Bose, R.; Ghosh, P.; Tripathi, V. J.; Ray, A. B.; Dasgupta, B. Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India **Psychopharmacological studies on (-)-nuciferine and its Hofmann degradation product atherosperminine.** Psychopharmacology (Berlin). 59(1):29-33, 1978.

The effects of (--)-nuciferine and its Hofmann degradation product atherosperminine on dopamine receptor activity were examined in adult albino rats and mice. Nuciferine showed a pharmacological profile of action associated with dopamine receptor blockade; it induced catalepsy and inhibited spontaneous motor activity, conditioned avoidance response, amphetamine toxicity, and stereotypy. Atherosperminine, by contrast, produced effects associated with dopamine receptor stimulation; produced stereotypy, increased spontaneous motor activity and amphetamine toxicity, reversed haloperidol-induced catalepsy and inhibition of conditioned avoidance response, inhibited morphine analgesia, and potentiated the anticonvulsant action of diphenylhydantoin. Results are discussed in terms of the chemical configurations of the two compounds. 46 references. (Author abstract modified)

002825 Biggio, G.; Casu, M.; Corda, M. G.; Di Bello, C.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Stimulation of dopamine synthesis in caudate nucleus by intrastriatal enkephalins and antagonism by naloxone.** Science. 200(4341):552-554, 1978.

The effects of intraventricular injection of methionine-enkephalin or (D-A1a2)-methionine-enkephalinamide, a synthetic enkephalin analog resistant to enzyme degradation, on the stimulation of dopamine synthesis in the caudate nucleus of male Sprague-Dawley rats were examined. A marked dose dependent increase in dihydroxyphenylacetic acid and homovanillic acid concentrations occurred. The (D-A1a2) analog increased the accumulation of dopa in the striatum after aromatic amino acid decarboxylase inhibition. At the highest doses used, both enkephalins failed to modify brain serotonin metabolism. The monolateral microinjection of the (D-A1a2) analog into the caudate nucleus increased the concentration of dihydroxyphenylacetic acid in the injected side, whereas bilateral injection increased the concentration of this compound in both caudate nuclei and caused catalepsy. The stimulant effect on dopamine synthesis persisted after destructin of striatal postsynaptic dopamine receptors with kainic acid. The biochemical and behavioral effects of enkephalins were prevented by naloxone. Results indicate

that enkephalins stimulate dopamine synthesis by an action on opioid receptors localized on dopaminergic nerve terminals. 20 references. (Author abstract modified)

002826 Biggio, G.; Corda, M. G.; Casu, M.; Salis, M.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Italy **Disappearance of cerebellar cyclic GMP induced by kainic acid.** Brain Research (Amsterdam). 154(1):203-208, 1978.

The effect of intracerebellar injection of kainic acid on the cyclic 3',5'-guanosine monophosphate (GMP) content of the cerebellar cortex was investigated in male Sprague-Dawley rats. Kainic acid caused a marked initial increase in cyclic GMP content, followed by a persistent loss of the nucleotide; this indicates that the cerebellar cyclic GMP system is localized in selectively stimulated neurons, which are then destroyed by kainic acid. The selective destruction of these neurons by kainic acid also prevented the increase of cyclic GMP in the cerebellar cortex elicited by isoniazid and harmaline. 22 references.

002827 Biggio, G.; Corda, M. G.; Casu, M.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Italy **Effect of chronic treatment with neuroleptics on the content of 3',5'-cyclic guanosine monophosphate in cerebellar cortex of rats.** Life Sciences (Oxford). 23(6):649-652, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the effect of chronic treatment with haloperidol on the content of cyclic guanosine monophosphate (cGMP) in the cerebellar cortex of male Sprawgue-Dawley rats is reported. Administration of 0.5mg/kg haloperidol decreased cerebellar cGMP by 80% in control rats but failed to alter the nucleotide content in rats chronically treated with haloperidol (0.5mg/kg twice daily for 20 days). A dose of 0.5mg/kg apomorphine enhanced cGMP by 25% in control rats and by 60% in rats chronically treated with haloperidol. Results suggest that there is a functional link between the striatum and cerebellum and that cerebellar cGMP is a sensitive indeed of the state of activation of striatal dopamine receptors. 9 references. (Author abstract modified)

002828 Biggio, G.; Corda, M. G.; Casu, M.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Cagliari Italy **Decrease of cyclic GMP in cerebellum by intrastriatal D-Ala2-Met-Enkephalinamide.** Life Sciences. 23(4):335-340, 1978.

The bilateral intrastriatal injection of D-Ala2-Met-Enkephalinamide (DALA) at doses ranging from 12 to 50mcg decreased cyclic guanosine monophosphate (GMP) content in the cerebellum and produced catalepsy in male Sprague-Dawley rats. These effects were prevented by naltrexone, an opiate receptor antagonist, but not by apomorphine, a dopamine agonist. The bilateral injection of DALA in the cerebellum and substantia nigra neither decreased cerebellar cyclic GMP content nor produced catalepsy. The bilateral injection of DALA (20mcg) into the ventromedial thalamic nuclei caused marked catalpesy but failed to decrease cerebellar cyclic GMP. Results suggest that the effect of DALA on cyclic GMP can be differentiated from the cataleptic response and that it is mediated by an action on opioid receptors located in the striatum, beyond the dopamine receptors. 14 references. (Author abstract)

002829 Bioulac, B.; Boulard, G.; Vincent, J.-D.; Puil, E. Laboratoire de Neurophysiologie, Universite de Bordeaux II, 146 rue Leo Saignat, F-33076, Bordeaux Cedex, France **Effects of dopamine agonists on neurones in the caudate nucleus and cerebral cortex of cats chronically treated with neuroleptics.** Neuropharmacology (Oxford). 17(11):965-969, 1978.

The hypothesis that chronic administration of neuroleptics interrupts dopaminergic transmission and thereby allows the development of supersensitivity at postsynaptic dopamine (DA) receptor sites was tested. DA and the DA agonists apomorphine and piribedil were applied microiontophoretically to caudate and cortical neurons of cats chronically treated with chlorpromazine or haloperidol for 6 months. No siginificant differences in neuronal sensitivity to DA and DA agonists were observed in normal and neuroleptic treated cats. 20 references. (Author abstract modified)

002830 Bioulac, Barnard; Gaffori, Odile; Harris, Martin; Vincent, Jean-Didier. Laboratoire de Neurophysiologie, Universite de Bordeaus II, France **Effects of acetylcholine, sodium glutamate and GABA on the discharge of supraoptic neurons in the rat.** Brain Research (Amsterdam). 154(1):159-162, 1978.

The effects of acetylcholine (ACh), sodium glutamate (GLU), and gamma-aminobutyric acid (GABA) on the discharge of slow continuous and phasic hypothalamic supraoptic neurons were examined in Wistar rats. Of the slow continuous neurons, 99 were inhibited by iontophoretic applicatin of ACh, 14 were excited, and 11 were unaffected. Application of GLU resulted in excitation of these neurons, while GABA produced inhibition; these effects lasted only so long as the iontophoretic current was applied. The responses of phasic neurons to ACh, GLU, and GABA differed markedly from those of slow continuous neurons; the effects of these substances differed according to whether they were applied when the neuron was silent or during discharge. The contrasting effects of ACh, GLU, and GABA on the discharge of slow continuous (oxytocin) and phasic (vasopressin) neurons suggest that ACh is the transmitter for vasopressin release and emphasize the complex nature of the control of phasic discharge. 9 references.

002831 Biscoe, T. J.; Davies, J.; Dray, A.; Evans, R. H.; Martin, M. R.; Watkins, J. C. Department of Physiology, Medical School, University of Bristol, Bristol BS8 1TD, England **D-alpha-aminoadipate, alpha,epsilon-diominopimelic acid and HA-966 as antagonists of amino acid-induced and synaptic excitation of mammalian spinal neurones in vivo.** Brain Research (Amsterdam). 148(2):543-548, 1978.

The effects of D-alpha-aminoadipate, alpha,epsilon-diaminopimelic acid, and HA-966 (3-amino-1-hydroxy-2-pyrrolidone) on amino acid-induced and synaptic excitation of mouse and cat spinal interneurons were examined. All three agents markedly antagonized N-methyl-D-aspartate (NMDA)-induced excitation of dorsal horn interneurons, with little or no effect on kainate-induced excitation of these cells. Excitatory responses to L-glutamate and L-aspartate were also depressed by the three agents used, and all three agents effectively suppressed synaptic excitation. D-alpha-aminoadipate showed the greatest specificity for antagonism of NMDA-induced neuronal excitation. 10 references.

002832 Biswas, Bratati; Carlsson, Arvid. Department of Pharmacology, University of Goteborg, Goteborg, Sweden **Potentiation by neuroleptic agents of the inhibitory action of intraperitoneally administered GABA on the locomotor activity of mice.** Pharmacology Biochemistry and Behavior. 8(6):651-654, 1978.

The action of gamma-aminobutyric acid (GABA) as potentiated by neuroleptic drugs in female NMRI mice was studied. A number of neuroleptic agents were shown to be capable of potentiating the inhibitory action of intraperitoneally administered GABA. Haloperidol, chlorpromazine, thioridazine, and clozapine are shown to possess such ability. Spiperone, which is considered to be highly selective in blocking dopamine receptors, was an ineffective neuroleptic in this case. Phenoxybezamine

also proved active in potentiating GABA. It is concluded that blockage of dopamine receptors as well as alpha-adrenergic receptors may be responsible for neuroleptic-induced potentiation of GABA actions. 8 references. (Author abstract modified)

002833 Blatchford, D.; Holzbauer, Margarethe; Ingram, D. L.; Sharman, D. F. Agricultural Research Council Institue of Animal Physiology, Babraham, Cambridge CB2 4AT, England **Responses of the pituitary-adrenal system of the pig to environmental changes and drugs.** British Journal of Pharmacology (London). 62(2):241-254, 1978.

The reactivity of the pituitary-adrenal axis of the young pig was tested for its suitability as a sensitive index for discomfort that might be experienced under certain conditions of intensive husbandry. Stimuli such as exposure to ambient temperatures of 40 degrees C or minus 5 degrees C were required to cause large rises in plasma concentrations of adrenocorticotroic hormone (ACTH) and corticosteroids. Apparently milder stimuli, such as change of environment, slight frustration or changes in ambient temperatures between 5 and 30 degrees C rarely caused a significant rise in plasma corticosteroids. Thus changes in plasma corticosteroid concentrations are not a sensitive index for the reaction of a piglet to its environment. Increases in plasma ACTH concentrations occurred faster than those of the corticosteroids, were proportionately larger, and occurred following relatively small disturbances. Thus rises in plasma ACTH might be a useful indication that a given situation is disturbing to a pig. Azaperone, a drug which is used as a sedative in pigs, caused a rise of about 50% in plasma corticosteroid concentrations but did not diminish the large steroid output seen when the animals were exposed to high and low ambient temperatures. 20 references. (Author abstract)

002834 Bloom, Alan S.; Dewey, William L. Department of Pharmacology, Medical College of Wisconsin, Milwaukee, WI 53233 **A comparison of some pharmacological actions of morphine and delta9-tetrahydrocannabinol in the mouse.** Psychopharmacology (Berlin). 57(3):243-248, 1978.

The effects of morphine and delta9-tetrahydrocannabinol (THC) on the tail flick reflex, body temperature, and catecholamine synthesis were examined in male ICR strain mice. Both morphine and THC produced antinociception, hypothermia, and increased catecholamine synthesis 30 minutes after subcutaneous injection. Morphine produced greater increases in dopamine synthesis and was a more potent antinociceptive agent, while THC produced greater increases in norepinephrine synthesis and was a more potent hypothermic agent. Naloxone pretreatment partially antagonized the hypothermia and increase in catecholamine synthesis produced by THC. Asymmetric cross tolerance between morphine and THC was observed; THC tolerant animals were cross tolerant only to the hypothermic action of morphine, and morphine tolerant animals were cross tolerant only to the antinociceptive action of THC. It is suggested that these studies may be of general significance in view of the frequent simultaneous use of these classes of drugs by humans and the proposed use of THC for treatment of the narcotic abstinence syndrome. 29 references. (Author abstract modified)

002835 Bloom, Alan S.; Johnson, Kenneth M.; Dewey, William L. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **The effects of cannabinoids on body temperature and brain catecholamine synthesis.** Research Communications in Chemical Pathology and Pharmacology. 20(1):51-57, 1978.

The correlation between the hypothermic effects of several naturally occurring and synthetic cannabinoids and their effects on the synthesis of dopamine and norepinephrine was examined in ICR mouse brain. Delta9-tetrahydrocannabinol, 11-OH-delta9-tetrahydrocannabinal and 9-nor-9beta-OH-hexahydrocannabinol produced hypothermia and increased catecholamine synthesis in mouse brain. Results indicate that the potencies of the effects of these compounds were correlated. Cannabinol and cannabidiol were found to be inactive in both tests. 12 references. (Author abstract modified)

002836 Blosser, James C.; Myers, Paul R.; Shain, William. Department of Neurology, Baylor College of Medicine, Houston, TX 77030 **Neurotransmitter modulation of prostaglandin E1-stimulated increases in cyclic AMP. I. Characterization of a cultured neuronal cell line in exponential growth phase.** Biochemical Pharmacology (Oxford). 27(8):1167-1172, 1978.

Two sympathetic ganglion cell X neuroblastoma somatic cell hybrids, TCX 11 and TCX 17, were found to have a prostaglandin E1 (PGE1) sensitive adenylyl cyclase that was inhibited in whole cells by carbachol, norepinephrine (NE), and dopamine (DA). Serotonin and morphine were without effect. In the TCX 17 clone, carbachol produced a greater degree of inhibition than NE or DA. The inhibition by carbachol could be reversed by the muscarinic antagonists scopolamine and atropine, while the nicotinic antagonists alpha-bungarotoxin and d-tubocurarine were without effect. The inhibition by NE and DA was mimicked by phenylephrine but not by isoproterenol, apomorphine, or ET495. The alpha-antagonists phenoxybenzamine and phentolamine reversed the inhibition by NE and DA. Chlorpromazine reversed the inhibition of cyclic adenosine monophosphate formation by DA. Trifluoperazine and fluphenazine had no effect. It is concluded that the TXC 17 clone expresses two classes of receptors capable of modulating PGE1; the cholinergic receptor is muscarinic and the catecholamine receptor has alpha-adrenergic properties. 35 reference. (Author abstract modified)

002837 Bosin, Talmage, R.; Baldwin, John R.; Maickel, Roger P. Section on Pharmacology, Medical Sciences Program, Indiana University School of Medicine, Bloomington, IN 47401 **Inhibition of DOPA decarboxylation by analogues of tryptophan.** Biochemical Pharmacology (Oxford). 27(8):1289-1291, 1978.

The activity of several analogues of tryptophan as inhibitors of the decarboxylation of L-DOPA was examined. The benz (b)thiopoene analogue of 5-hydroxytryptophan was the most potent inhibitor of DOPA decarboxylation, followed in order by alpha-methyl-DOPA and the benzo(b)thiophene and 1-methylindole analogues of tryptophan. Tryptophan itself was inactive. These results are consistent with previous findings that a 5-hydroxy function considerably increases the affinity of tryptophan for the enzyme. 30 references.

002838 Bowery, N. G.; Dray, A. Department of Pharmacology, St. Thomas's Hospital Medical School, London SE1 7EH, England **Reversal of the action of amino acid antagonists by barbiturates and other hypnotic drugs.** British Journal of Pharmacology (London). 63(1):197-215, 1978.

The effects of barbiturates and other sedative/hypnotic drugs were examined in relation to gamma-aminobutyric acid (GABA) in vitro in the superfused isolated superior cervical ganglion of the Wistar rat and in vivo in single units in the brainstem of anesthetized rats. The barbiturates and other hypnotics prevented or reversed the actions of GABA antagonists and to a lesser extent the glycine antagonist, strychnine. It is suggested that the reversal exhibited by these drugs may be explained by assuming that the amino acids and their antagonists bind to the membrane at a separate site. It is concluded that if the reversal agent has particular affinity only for the antagonist binding site, it may

displace the antagonist without affecting the receptor. 55 references. (Author abstract modified)

002839 Bradford, H. F.; Ward, H. K.; Thomas, A. J. Dept. of Biochemistry, Imperial College, London, SW7 2AZ, England **Glutamine -- a major substrate for nerve endings.** Journal of Neurochemistry (Oxford). 30(6):1453-1459, 1978.

The metabolism of glutamine and the effects on glutaminase activity of a range of cytoplasmic constituents of synaptosomes was examined. Mammalian cortical synaptosomes incubated in the presence of glucose (2.5mM) plus glutamine (0.5mM) showed a 30% increase in transmitter amino acid content over controls with glucose alone and a doubling of glutamate release induced by Veratrine or high K. Double label experiments, i.e.,U-14C glucose with 3H glutamine, and single label experiments, i.e.,U-14C glucose or U-14C glutamine shoed that stimulus released glutamine derived principally (80%) from glutamine. Released glutamine derived glutamate was of higher specific radioactivity than its tissue equivalent. Glutamine alone (0.5-0.75 mM) was much less effective than equivalent amounts of glucose alone, in stimulating respiration and maintaining tissue K levels. 21 references. (Author abstract)

002840 Braestrup, Claus; Nielsen, Mogens. Psychopharmacological Research Laboratory, St. Hans Mental Hospital, Department E, DK-4000 Roskilde, Denmark **Ontogenetic development of benzodiazepine receptors in the rat brain.** Brain Research (Amsterdam). 147(1):170-173, 1978.

The ontogenetic development of brain benzodiazepine receptors was investigated in Wistar rats. Specific (3H)diazepam binding was present 8 days before birth in a concentration of 1.49pmol/g tissue, or 5.2% of the adult concentration; the total number of receptors per brain was only 0.1% of the maximal adult number. At birth, the receptor concentration was 35.4% of the adult level, and the total number of receptor sites was 2.5% of the total number in adults. Within the first week after birth, an almost maximal concentration of receptors was reached. During the first 3 weeks after birth, the total number of receptors increased steadily to a plateau of about 55pmol/brain, which was reached about 4 weeks after birth. Qualitative receptor characteristics, such as the apparent affinity constants and the concentrations of diazepam or clonazepam required to inhibit (3H)diazepam binding, did not change with development. 13 references.

002841 Bramwell, G. J.; Bradley, P. B. no address **Effects of morphine on brainstem neurones in naive and chronic morphine-treated rats, and effects of PCPA.** Neuropharmacology (Oxford). 17(11):975-978, 1978.

The effects of morphine and p-chlorophenylalanine (PCPA) on brainstem neurons in naive and morphine dependent male Sprague-Dawley rats were investigated. Overall responsiveness of brainstem neurons to morphine was not affected by 7 days of morphine exposure. However, a small reduction in the proportion of morphine-induced depressions was observed in chronic morphine-treated rats compared to controls. Animals withdrawn from morphine did not show this difference. Chronic morphine treatment also increased the incidence of naloxone-induced excitation. Pretreatment with PCPA reduced the overall responsiveness of naive animals to morphine, but increased the proportion of morphine excitations in chronic morphine treated animals. 19 references. (Author abstract modified)

002842 Breyer-Pfaff, Ursula; Spribille, Thomas; Jahns, Ilse. Department of Toxicology, University of Tuebingen, Germany **Influence of phenobarbital on the distribution and elimination of desmethylimipramine in the rat.** Biochemical Pharmacology (Oxford). 27(11):1521-1526, 1978.

The effect of oral pretreatment with phenobarbital (PB) on the distribution and elimination of desmethylimipramine (DMI) was investigated in male Wistar rats. Following intraperitoneal injection of 25mg/kg DMI, levels of DMI declined steadily with a half life of 6-7 hours in brain, liver, kidney, and plasma. Oral pretreatment with PB for 5 days enhanced DMI elimination slightly and decreased brain/plasma concentration ratios. Results are discussed in relation to the problem of antidepressant/barbiturate interactions in psychiatric therapy. 30 references. (Author abstract modified)

002843 Briley, M.; Langer, S. Z. Synthelabo, L.E.R.S., Department of Biology, Synaptic Receptor Group, 58, rue de la Glaciere, F-75013 Paris, France **Two binding sites for 3H-spiroperidol on rat striatal membranes.** European Journal of Pharmacology (Amsterdam). 50(3):283-284, 1978.

Two binding sites for (3H)spiroperidol on rat striatal membranes were demonstrated. Scatchard plots of the binding of (3H)spiroperidol (0.05-20nM) to rat striatal membranes repeatedly showed two components with dissociation constraints (0.17 and 1.32nM) differing by a factor of about eight. The higher affinity component comprised 41.4% of the total specific binding, which was 290fmoles/mg protein. Both binding sites were displaced by neuroleptics such as haloperidol (inhibitory constants 0.09 and 0.95nM) amd by dopamine receptor agonists such as dopamine (inhibitory constants 3.6and 30mcM) and apomorphine (inhibitory constants 0.09 and 5.88mcM). Both sites were stereospecific, with ()butaclamol being approximately 1000 times more potent than (-)butaclamol at displacing (3H)spiroperidol from each site. These results demonstrate the importance of studying the binding of the radioactive ligand and the displacing drugs over a wide range of concentrations. Clarifications of the physiological significance of the two types of neuroleptic binding sites may elucidate the role of central dopaminergic transmission and neuroleptics in the treatment of schizophrenia. 5 references.

002844 Brown, D. A.; Constanti, A. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Interaction of pentobarbitone and gamma-aminobutyric acid on mammalian sympathetic ganglion cells.** British Journal of Pharmacology (London). 63(1):217-224, 1978.

Interactions of bath applied pentobarbitone and gamma-aminobutyric acid (GABA) on neurons in the isolated superior cervical ganglia of the Wistar rat were examined with intracellular microelectrodes. Pentobarbitone itself (30mcM-1mM) showed no clear or consistent GABA-like effects; changes in resting input conductance and membrane potential were small and variable. Pentobarbitone (100mcM) strikingly enhanced the conductance increases produced by GABA and 3-aminopropanesulphonic acid and reversed the depression of GABA evoked responses by bicuculline. It is concluded that reversal of bicuculline action at the membrane conductance level might be explained by augmentation of GABA action. This augmentation cannot be attributed to partial agonist properties of pentobarbitone or to interference with glial transport processes. 22 references. (Author abstract)

002845 Browning, R. A.; Simonton, R. L. School of Medicine, Southern Illinois University, Carbondale, IL 62901 **Antagonism of the anticonvulsant action of phenytoin, phenobarbital, and acetazolamide by 6-hydroxydopamine.** Life Sciences. 22(21):1921-1930, 1978.

The ability of phenytoin, phenobarbital, and acetazolamide to prevent the tonic extensor component of the maximal electroshock seizure was evaluated in male Sprague-Dawley rats 30-50

days after treatment with 6-hydroxydopamine (6-OHDA). With all three drugs, protection of rats from tonic extension was markedly reduced in the catecholamine deficient animals. However, the 6-OHDA-induced antagonism of anticonvulsant action could be overcome by increasing the dose of the anticonvulsants. These findings suggest a nonspecific antagonism of anticonvulsant action in 6-OHDA treated rats, probably resulting from the increase in seizure susceptibility associated with catecholamine depletion. 25 references. (Author abstract modified)

002846 Brunner, Robert L.; Vorhees, Charles V.; McLean, Maria S.; Butcher, Richard E.; Berry, Helen K. Institute for Developmental Research of the Children's Hospital Research Foundation, Cincinnati, OH 45229 **Beneficial effect of isoleucine on fetal brain development in induced phenylketonuria.** Brain Research (Amsterdam). 154(1):191-195, 1978.

Dietary isoleucine (3%) significantly reduced the degree of growth retardation normally observed in fetuses from pregnant Spargue-Dawley rats fed a phenylketonuria inducing diet. No changes were seen in maternal bodyweight or food consumption or in fetal or maternal plasma phenylalanine levels as a result of isoleucine supplementation. Other amino acids tested (valine, leucine, methionine, tryptophan, threonine, aspartic acid, and tyrosine) did not provide the protective effects observed with isoleucine. 13 references.

002847 Burgess, E. J.; Atterwill, C. K.; Prince, A. K. Dept. of Pharmacology, King's College, Strand, London, WC2R 2LS, England **Choline acetyltransferase and the high affinity uptake of choline in corpus striatum of reserpinised rats.** Journal of Neurochemistry (Oxford). 31(4):1027-1033, 1978.

Striatal sodium dependent high affinity uptake of choline and choline acetyltransferase activity were investigated in reserpinized rats. Rats treated with reserpine show increased Vmax for the high affinity uptake of choline into small slices of corpus striatum; choline acetyltransferase activity of whole homogenates of striatum also was increased. These changes are consistent with increased cholinergic neuronal activity in the striatum and are considered to be likely adaptations mediating increased rates of synthesis of acetylcholine. 60 references. (Author abstract modified)

002848 Burkard, Willy P. Pharmaceutical Research Department, F. Hoffman-La Roche & Co. Ltd., CH-4002 Basle, Switzerland **Histamine H2-receptor binding with 3H-cimetidine in brain.** European Journal of Pharmacology (Amsterdam). 50(4):449-450, 1978.

Specific binding of 3H-cimetidine, which may label histamine H2 receptors, was demonstrated in guinea-pig brain. Two H2 antagonists, cimetidine and metiamide, inhibited binding by 50% at 27 and 45nM, respectively. Compounds chemically related to the H2 antagonists, as well as the alpha-adrenergic blocking agents tolazoline and phentolamine, were several hundred times less potent in inhibiting 3H-cimetidine binding. All other drugs tested, including H1 antihistaminics and specific H1 or H2 agonists were at least 1000 times less potent than the two H2 antagonists. It is concluded that the characteristics of the specific 3H-cimetidine binding site may indicate the presence of histamine H2 receptors in mammalian brain. 5 references.

002849 Burki, H. R.; Asper, H.; Ruch, W.; Zuger, P. E. Research Institute, Wander Ltd., P.O. Box 2747, CH-3001 Berne, Switzerland **Bromocriptine, dihydroergotoxine, methysergide, d-LSD, CF 25-397, and 29-712: effects on the metabolism of biogenic amines in the brain of the rat.** Psychopharmacology (Berlin). 57(3):227-237, 1978.

The effects of the ergolene derivatives bromocriptine, dihydroergotoxine, methysergide, d-lysergic acid diethylamide (LSD), 9,10-didehydro-6-methyl-8beta-(2-pyridylthiomethyl)-ergolene tartrate (CF 25-397), and 6-methyl-8alpha-cyanomethyl-ergoline methanesulphonate (29-712) on the metabolism of the biogenic amines in the brain were investigated in male Sprague-Dawley rats. All six ergolene derivatives increased the concentration of 4-hydroxy-3-methoxyphenylethylene glycol sulphate in the brain stem. In brain homogenates, the agents inhibited the binding of 3H-dihydroergocryptine to alpha-adrenoreceptors but only weakly inhibited the binding of 3H-alprenolol to beta-adrenoreceptors. All the ergolenes increased the concentration of serotonin in the cortex, but only bromocriptine and 29-712 increased the concentration of 5-hydroxyindoleacetic acid (5-HIAA). Reserpine-induced pontogeniculooccipital waves in the rat were inhibited by all six compounds. Bromocriptine, 29-712, and, to a much lesser extent, dihydroergotoxine reduced the concentration of 3,4-dihydroxyphenylacetic acid (DOPAC). CF 25-397 caused a slight increase in DOPAC concentration at high doses, and LSD and methysergide caused pronounced increases. At doses lower than 1mg/kg, LSD decreased the DOPAC concentration. 31 references. (Author abstract modified)

002850 Burstein, Sumner; Hunter, Sheila A. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Prostaglandins and cannabis -- VI. Release of arachidonic acid from HeLa cells by delta1-tetrahydrocannabinol and other cannabinoids.** Biochemical Pharmacology (Oxford). 27(8):1275-1280, 1978.

Treatment of HeLa cells in suspension culture with (14C)arachidonic acid led to a rapid incorporation of this fatty acid into cellular phospholipid pools. Exposure of these labeled cells to delta1-tetrahydrocannabinol and other cannabis constituents led to a dose related release of arachidonic acid into the culture medium. Cannabinol and cannabichromene were also effective, whereas other cannabinoids were less potent and non-cannabinoid constituents such as eugenol were without activity. This action of the cannabinoids could have direct effects on cell membrane structure and could alter the biosynthesis of prostaglandins and related metabolites of arachidonic acid. 27 references. (Author abstract)

002851 Butcher, Larry L.; Rogers, Richard C. Department of Psychology, University of California, 405 Hilgard Avenue, Los Angeles, CA 90024 **Histochemical effects of kainic acid on neostriatal dopamine and acetylcholinesterase.** European Journal of Pharmacology (Amsterdam). 50(3):287-289, 1978.

The histochemical effects of kainic acid on neostriatal dopamine (DA) and acetylcholinesterase (AChE) were investigated in female Sprague-Dawley rats. Different zones of pathology, occurring successively in relation to the injection cannula, could be discerned after intrastriatal administration of kainate: a zone of complete destruction of neuronal, glial, and vascular elements due to tissue displacement by the injection cannula; a region of virtually total loss of neuronal elements regardless of chemical characteristics (Z2); and an area in which different subcellular constituents of neurons were differentially affected (Z3). AChE decreased in Z3 after exposure to kainic acid, while DA levels in a subtotal population or neuronal elements in that region first increased and then decreased over a 15 day period. The number of DA elements in Z3 was clearly reduced, possibly due to degeneration, and no AChE or DA was observed in Z2. Results are discussed in relation to the limitations of kainic acid as a pharmacological tool. 5 references.

002852 Calderini, Gabriella; Carlsson, Arvid; Nordstrom, Carl-Henrik. Istituto di Ricerche Farmacologiche Mario Negri, Via Eritrea 62, I-20157 Milan, Italy **Influence of transient ischemia**

on monoamine metabolism in the rat brain during nitrous oxide and phenobarbitone anaesthesia. Brain Research (Amsterdam). 157(2):303-310, 1978.

Monoamine metabolism was studied during transient, incomplete ischemia of 15 minute duration in male Wistar rats maintained on 70% nitrous oxide or given 150mg/kg phenobarbitone. No changes in monoamine metabolism were observed during ischemia. Following 30 minutes of recirculation, increases in dopamine, 5-hydroxyindoleacetic acid, tyrosine, and tryptophan were found in both nitrous oxide and phenobarbitone treated animals. Pronounced postischemic decreases in norepinephrine and 5-hydroxytryptamine were found in animals anesthetized with nitrous oxide but not in those given phenobarbitone. During recirculation, the rate of tyrosine hydroxylation increased in striatum, limbic forebrain, and hemispheres, while tryptophan hydroxylation was reduced. Results suggest that neuronal activity is low or eliminated in dopaminergic and serotonergic neurons and high in noradrenergic neurons following transient, global cerebral ischemia. 19 references. (Author abstract modified)

002853 Cannon, J. G.; Costall, B.; Laduron, P. M.; Leysen, J. E.; Naylor, R. J. Division of Medicinal Chemistry and Natural Products, College of Pharmacy, University of Iowa, Iowa City, IA 52240 **Effects of some derivatives of 2-aminotetralin on dopamine-sensitive adenylate cyclase and on the binding of (3H) haloperidol to neuroleptic receptors in rat striatum.** Biochemical Pharmacology (Oxford). 27(10):1417-1420, 1978.

Putative dopamine (DA) agonists from a series of 2-aminotetralin derivatives were assessed for their ability to stimulate DA sensitive adeylate cyclase, to inhibit the binding of (3H)haloperidol to neuroleptic receptors in the striatum, and to stimulate motor function following intrastriatal or peripheral injection in female Wistar rats. Of the two primary amines, 2-amino-5,6-dihydroxytetralin and 2-amino-6,7-dishydroxytetralin, the 6,7-dihydroxy compound was found to be 20 times more potent than the corresponding 5,6-dihydroxytetralin derivative was the most active inhibitor of (3H)haloperidol binding, with 100 times the activity of DA. Agents most active in inducing DA-like motor effects following intrastriatal or subcutaneous injection were generally able to stimulate adenylate cyclase and to inhibit (3H)haloperidol binding; compounds that were inactive in behavioral tests were also inactive in the vitro tests. However, an absolute correlation between in vivo and in vitro potency could not be found. 16 references. (Author abstract modified)

002854 Carlsson, Christer; Johansson, Barbro B. MRC Cerebral Metabolism Group, E-Blocket, University Hospital, S-22185 Lund, Sweden **Blood-brain barrier dysfunction after amphetamine administration in rats.** Acta Neuropathologica (Berlin). 41(2):125-129, 1978.

In a study of blood-brain barrier dysfunction following amphetamine administration, it was found that amphetamine administration to rats anesthetized with nitrous oxide resulted in protein extravasation in the brain, particularly in the frontoparietal cortex. Protein leakage could be prevented by lowering the blood pressure, and also by hyperventilation. It is suggested that the permeability disturbance is caused by the mechanical stress which results from high intraluminal pressure in combination with vasodilatation. It is considered to be likely that the cerebral vasodilatation caused by amphetamine, at least in part, is secondary to an increased cerebral metabolism induced by a catecholamine release. 25 references. (Author abstract modified)

002855 Celuch, Stella M.; Dubocovich, Margarita L.; Langer, S. Z. Instituto de Investigaciones Farmacologicas, Conicet, Junin 956, 5 Piso, Buenos Aires, Argentina **Stimulation of presynaptic beta-adrenoceptors enhances (3H)-noradrenaline release during nerve stimulation in the perfused cat spleen.** British Journal of Pharmacology (London). 63(1):97-109, 1978.

The effects of isoprenaline, propranolol, and phosphodiesterase inhibitors on 3H-norepinephrine (NE) overflow elicited by low frequency nerve stimulation were determined in the isolated perfused spleen of the cat. (-)-Isoprenaline produced a concentration dependent increase in NE overflow evoked by nerve stimulation at 1 Hz and was more effective at 1 Hz than at 2 Hz. A concentration of propranolol (0.1mcM) devoid of neuron blocking activity blocked this effect of isoprenaline. ()-Isoprenaline (140nM) failed to increase the release of radioactivity induced by nerve stimulation. The increase in NE overflow induced by nerve stimulation during exposure to the phosphodiesterase inhibitor, papaverine (27mcM), was more pronounced than that obtained in the presence of 3-isobutyl-1-methyl xanthine (0.5mM). In the presence of papaverine, the concentration/effect curve for (-)-isoprenaline on transmitter release was shifted to the left and its maximum increased. It is concluded that activation of presynaptic beta-adrenoceptors in the perfused cat spleen leads to an enhancement in transmitter release that appears to be linked to an increase in cyclic adenosine monophosphate levels in noradrenergic nerve endings. 44 references. (Author abstract modified)

002856 Cerletti, Chiara; Coccia, P.; Manara, L.; Mennini, Tiziana; Recchia, M. Laboratory of Drug Metabolism, Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea, 62, 20157 Milan, Italy **Subcellular distribution of etorphine in rat brain and evidence for in vivo stereospecific binding.** British Journal of Pharmacology (London) 62(1):31-38, 1978.

The subcellular distribution in male Sprague-Dawley rat brain of rediolabelled etorphine given intravenously was studied. Subcellular fractionation of a 0 degree centigrade homogenate of rat brain containing various concentrations of tritiated etorphine showed that the distribution of the drug among the primary fractions was dependent on the contration of etorphine. The brains of rats injected intravenously with 0.2and 20mcg/kg of radiolablled etorphine were homogenized and fractionated in sucrose containing 4.2times ten to the minus 5 M unlabelled etorphine in order to control redistribution artifacts. Different distribution profiles in the subcellular fractions were observed at these two dose levels. Concurrent administration of either cyprenorphine or noloxone with intravenous etorphine caused a shift of the labelled drug from the P3 fraction to the supernatant fraction. The subcellular distribution of intravenously administered labelled etorphine was also studied by homogenizing brains in etorphine free sucrose, and sucrose containing either levorphanol or dextrorphan. These experiments indicate that the P3 microsomal fraction is a major site to which in vivo etorphine is sterospecifically bound in the rat brain. 32 references. (Author abstract modified)

002857 Chalfie, Martin; Settipani, Laurel; Perlman, Robert L. Department of Physiology, Harvard Medical School, Boston, MA 02115 **Activation of tyrosine 3-mono-oxygenase in pheochromocytoma cells by lasalocid.** Biochemical Pharmacology (Oxford). 27(5):673-677, 1978.

Tyrosine 3-mono-oxygenase (TH) activity was measured in extracts of cells prepared from a transplantable rat pheochromocytoma. Incubation of the cells with the ionophore lasalocid resulted in an increase in TH activity. The activation of TH by lasalocid was associated with an increase in the maximum velocity of the enzyme but was not accompanied by a change in the apparent Michaelis-Menten constant of the enzyme for its pteridine cofactor or for tyrosine. In these respects, the activation of TH by lasalocid resembles that produced by incubation of the

cells in media containing 56mM potassium ion. This effect of lasalocid was not dependent on the presence of extracellular calcium ions. It is suggested that the activation of TH by lasalocid may be mediated by the ionophore-induced release of calcium ions from some intracellular store. 27 references. (Author abstract)

002858 Chaloupka, Z.; Rokyta, R.; Sobotka, P.; Vencovsky, E. Dept. of Pathological Physiology, Medical Faculty, Charles University, Lidicka 1, Plzen, Czechoslovakia **Short- and long-term effects of cerebrolysine on evoked cortical potentials in rats.** Activitas Nervosa Superior (Praha). 20(1):83, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, short-term and long-term effects of cerebrolysine on evoked cortical potentials in rats are described. Neither chronic nor acute dosage with cerebrolysine had an appreciable effect on cortical evoked potentials in rats. 2 references.

002859 Chee, Po Yok; Dahl, June L. Dept. of Pharmacology, University of Wisconsin, Madison, WI 53706 **Measurement of protein turnover in rat brain.** Journal of Neurochemistry (Oxford). 30(6):1485-1493, 1978.

Degradation rates of rat brain proteins were measured by following the decay in specific radioactivity of carboxyl labelled aspartate and glutamate over a 17 day period. Initial labelling of these amino acids was achieved by a single intraperitoneal injection of NaH14CO3. The nonlinear decay curve for total brain proteins could be approximated by assuming that the mixture contained two classes of proteins with half lives of 3.3and 8.7days, respectively. Half lives of 2.5and 7.7days were estimated for such protein classes in the microsomal fraction. The half lives of soluble proteins, synaptic membranes, cell body and synaptic mitochondria were 3.1, 5.8, 5.6and 8.4days, respectively. Identical results were obtained if the change in specific activity of intact protein labeled by NaH14CO3 was followed. Two fold slower decay rates were obtained when brain proteins were labeled with a pulse of (4,5-3H)leucine or (1-14C)leucine. Half lives calculated for the two classes of proteins in whole brain were 8.4and 16.5days, respectively, with (4,5-3H)leucine and 8.9and 14.2days, respectively with (1-14C)leucine. These results indicate the very significant reutilization of this amino acid in brain. Sodium (14C)bicarbonate is a more satisfactory isotopic precursor for accurate assessment of rates of protein turnover in brain. 26 references. (Author abstract)

002860 Cheng, S. -C.; Naruse, H.; Brunner, E. A. Dept. of Anesthesia, Northwestern University Medical School, 303 E. Chicago Ave., Chicago, IL 60611 **Effects of sodium thiopental on the tricarboxylic acid cycle metabolism in mouse brain: CO2 fixation and metabolic compartmentation.** Journal of Neurochemistry (Oxford). 30(6):1591-1593, 1978.

In a study of the effects of sodium thiopental on the tricarboxylic acid cyle metabolism in mouse brain, the effects of sodium thiopental on CO2 fixation suggest that anesthetic agents have inhibitory effects on a hypothesized large metabolic compartment and stimulating effects on the small metabolic compartment. The selective thiopental induced increases in aspartate (and malate) specific radioactivity and in the flutamine/glutamate specific radioactivity ratio in mouse brain during CO2 fixation are consistent with the two compartment hypothesis. 21 references.

002861 Cheng, Sze-Chuh; Brunner, Edward A. Dept. of Anesthesia, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL 60611 **Alteration of tricarboxylic acid cycle metabolism in rat brain slices by halothane.** Journal of Neurochemistry (Oxford). 30(6):1421-1430, 1978.

A study of the alteration of the tricarboxylic acid cycle (TCAC) metabolism in rat brain slices due to halothane was conducted. TCAC included in the experiments were: 1c acetylcholine (ACh), citrate, glutamate, glutamine, gamma-aminobutyrate (GABA) and aspartate. The trichloracetic acid soluble extract, the trichloroacetic acid insoluble precipitate and its lipid extract were also studied. In control experiments, pyruvate preferentially labelled ACh, citrate, glutamate, GABA and aspartate. Acetate labeled AChe, but to lesser extent than pyruvate. Acetate also labeled lipids and glutamine. Citrate labeled lipids, but not ACh and served as a preferential precursor for glutamine. These data support a three compartment model for cerebral tricarboxylic acid cycle metabolism. Halothane caused increases in GABA and aspartate contents and a decrease in ACh content. It has no effect on the contents of citrate, glutamate, and glutamine. Halothane preferentially inhibited the metabolic transfer of radioactivity from pyruvate into almost all metabolites, and effect probably not related to pyruvate permeability. Halothane increase the metabolic transfer of radioactivity from citrate into the trichloracetic acid precipitate, lipids, and especially glutamine. Transfer of citrate radioactivity into GABA was somewhat decreased. The differential effects of halothane on acetate and citrate utilization suggest that the small metabolic compartment should be subdivided. Halothane did not interfere with the dicarboxylic acid portion of the tricarboxylic acid cycle. 53 references. (Author abstract)

002862 Chiueh, Chuang C.; Kopin, Irwin, J. GRC, Rm 3E19, Laboratory of Neurosciences, National Institute on Aging, Baltimore City Hospitals, Baltimore, MD 21224 **Radioenzymatic paper-chromatographic assay for dopamine and norepinephrine in cerebroventricular cisternal perfusate of cat following administration of cocaine or d-amphetamine.** Journal of Neurochemistry (Oxford). 31(2):561-564, 1978.

A sensitive radioenzymatic paper chromatographic procedure was used to measure the endogenous dopamine (DA) and norepinephrine content of cerebroventricular cisternal perfusate from cats, following administration of cocaine or d-amphetamine. Although relatively less potent than d-amphetamine, cocaine was shown to release endogenous catecholamines, mainly DA, from the brain. The similarity of cocaine and d-amphetamine in releasing DA from the brain may be the neurochemical basis for their similar behavioral effects. 33 references.

002863 Christian, C. N.; Nelson, P. G.; Bullock, P.; Mullinax, D.; Nirenberg, M. Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development, NIH, Bethesda, MD 20014 **Pharmacologic responses of cells of a neuroblastoma X glioma hybrid clone and modulation of synapses between hybrid cells and mouse myotubes.** Brain Research (Amsterdam). 147(2):261-276, 1978.

Cells of a neuroblastoma X glioma hybrid clone (NG108-15) responded to 5-hydroxytryptamine (5-HT), dopamine (DA), or acetylcholine (ACh) with graded depolarizations involving membrane conductance increases. Responses desensitized during continuous application of the neurotransmitters, and responses to 5-HT and DA cross-desensitized: a desensitizing application of one transmitter also desensitized the hybrid cell to the other neurotransmitter. ACh and 5-HT did not cross-desensitize. The hybrid cell response to 5-HT was not attenuated by D-lysergic acid diethylamide and was blocked by morphine, but not by binding to naloxone sensitive opiate receptors. Both 5-HT and the prostaglandin PGF2alpha caused the release of ACh at the synapses of hybrid cells with mouse myotubles and facilitated the synaptic release elicited by hybrid cell action protentials. Following treatment with the antimitotic agent cytosine arabinoside, co-cultures of hybrid cells and mouse myotubes exhibited plentiful synaptic connections only if maintained in medium con-

taining 1mM dibutyryl cyclic adenosine monophosphate (dBcAMP). After X-irradiation, co-cultures were synaptically active even in the absence of dBcAMP. 35 references. (Author abstract modified)

002864 Clark, Wesley G.; Cumby, H. Rick. Department of Pharmacology, Southwestern Medical School, University of Texas Health Science Center, Dallas, TX 75235 **Hyperthermic responses to central and peripheral injections of morphine sulphate in the cat.** British Journal of Pharmacology (London). 63(1):65-71, 1978.

The effect of morphine on body temperature was studied in conscious, unrestrained cats provided with implanted third or lateral cerebral ventricular cannulae, jugular venous catheters, and retroperitoneal thermocouples. Intraventricular injections of 2.5to 50mcg and intravenous injections of 1 to 10mg/kg morphine sulphate produced dose related hyperthermic responses. Similar mean increases in body temperature after morphine administration were elicited in cats that had not previously received morphine and in cats that received a series of injections of morphine spaced so as not to induce tolerance. Morphine was at least 850 times more potent when injected into the third ventricle than when given intravenously. Additional studies indicate that morphine increased the level at which body temperature was regulated. Since neither metiamide nor indomethacin antagonized morphine, histamine and prostaglandins were apparently not required for the hyperthermic effect. 19 references. (Author abstract modified)

002865 Claus, George; DeBernardo, Erica; Krisko, Istvan. University of Vienna Medical School, Vienna, Austria **Pilot study on the distribution of 14C-labeled methaqualone in the rat brain.** Biochemical Pharmacology (Oxford). 27(8):1300-1303, 1978.

The distribution of radioactive methaqualone in the brains of Wfu rats was studied, following oral administration of the drug. Peak tissue concentrations were found 3 hours after intubation. The highest concentrations appeared in the optic chiasm, pituitary gland, and reticular formation of the medulla oblongata. Serum concentrations were approximately one order of magnitude higher than those found in the brain. An apparently inert metabolite was found at 24 hours in concentrations double those of the peak tissue levels of the compound, both in the brains and in the sera. 22 references.

002866 Clemens, James A.; Fuller, Ray W.; Perry, Kenneth W.; Sawyer, Barry D. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Effects of p-chloroamphetamine on brain serotonin in immature rats.** Communications in Psychopharmacology. 2(1):11-15, 1978.

p-Chloroamphetamine and its effects on brain serotonin in Wistar immature rats were examined. p-Chloroamphetamine injection (20-50mg/kg, i.p.)depleted serotonin for up to 6 hours and for 1 to 2 weeks in the brains of 7-day-old to 20-day-old rats but not in 3-day-old to 5-day-old rats. Possible reasons for the iability of p-chloroamphetamine to deplete brain serotonin in newborn rats are considered. 13 references. (Author abstract modified)

002867 Clement-Cormier, Yvonne C.; Redburn, Dianna A. Department of Pharmacology, University of Texas Medical School, Health Sciences Center, Houston, TX 77025 **Dopamine-sensitive adenylate cyclase in retina -- subcellular distribution.** Biochemical Pharmacology (Oxford). 27(18):2281-2282, 1978.

Dopamine (DA) sensitive adenylate cyclase activity was localized in the P2 fraction of New Zealand rabbit retina, which is enriched in synaptosomes from amacrine cells and, to a lesser extent, from bipolar and horizontal cells. Adenylate cylase activity was also found in the P1 fraction, but adenylate cyclase sensitivity to DA was not associated with this fraction. The effects of various DA agonists and antagonists on adenylate cyclase activity in subcellular fractions revealed a high degree of pharmacological specificity for the receptor/cyclase complex. Results suggest that amacrine cells may stimulate adenylate cyclase systems within bipolar or ganglion cells by interacting with DA receptors that are pharmacologically similar to those previously characterized in the rat striatum. It is concluded that the fractionation procedure for the isolation of two synaptosomal preprations is an excellent model system for the study of all aspects of the DA system, including uptake, release, and cyclase activity. 22 references.

002868 Clineschmidt, Bradley V.; McGuffin, Jodie C. Merck Institue for Therapeutic Research, West Point, PA 19486 **Pharmacological differentiation of the central 5-hydroxytryptamine-like actions of MK-212 (6-chloro-2-(1-piperazinyl)-pyrazine), p-methoxyamphetamine and fenfluramine in an in vivo model system.** European Journal of Pharmacology (Amsterdam). 50(4):369-375, 1978.

Intravenous administration of 6-chloro-2-(1-piperazinyl)-pyrazine (MK-212, 0.1mg/kg), p-methoxyamphetamine (p-MA, 0.7mg/kg, or fenfluramine (2.5mg/kg) increased the frequency of twitches in the suprahyoideal muscle in male Sprague-Dawley rats. Xylamidine, a 5-hydroxytryptamine (5-HT) antagonist that penetrates poorly into the CNS, did not affect this action of MK-212, p-MA, or fenfluramine, but the centrally acting 5-HT antagonist methergoline abolished the effect of all three compounds. Pretreatment with fluoxetine caused a reduction in the abilities of p-MA and fenfluramine, but not MK-212, to increase twitch frequency. Inhibition of 5-HT synthesis with p-chlorophenylalanine (p-CPA) resulted in a marked diminution in the action of p-MA and an initial decrease in the activity of fenfluramine followed by a modest enhancement. The ability of MK-212 to increase the frequency of muscle twitching was greatly potentiated by treatment with p-CPA. Results suggest that all three compounds have a 5-HT-like action in the CNS. However, p-MA and fenfluramine appear to use the uptake system to gain access into the serotonergic neuron and then act indirectly via the release of 5-HT, whereas MK-212 acts directly on central 5-HT receptors. 20 references. 20 references. ('Author abstract modified)

002869 Clubley, Margaret. Wellcome Research Laboratories, Beckenham, Kent, England **The action of CNS drugs on an isolated sympathetic nerve preparation of rabbit.** European Journal of Pharmacology (Amsterdam). 50(3):175-181, 1978.

The effect of centrally active drugs on the transmission of nerve impulses through the isolated cervical symapthetic nerve and superior cervical ganglia of the New Zealand white rabbit was studied by recording both preganglionic and ganglionic responses to single square wave stimuli. Chlorpromazine, trifluoperazine, and haloperidol had a greater axonal depressant action than procaine and xylocaine. Chlordiazepoxide and diazepam were similar in local anesthetic potency to procaine, while meprobamate and sodium pentobarbitone showed only slight axonal depressant properties. It is concluded that meprobamate, sodium pentobarbitone, and possibly diazepam have ganglionic blocking properties, while procaine, chlorpromazine, trifluoperazine, haloperidol, and chlordiazepoxide reduce the ganglionic potential by virtue of their preganglionic action. The peripheral actions of centrally active drugs should not be ignored, since they may contribute to effects that are otherwise attributed to a central action. 11 references. (Author abstract modified)

002870 Cole, Francis E.; Frohlich, Edward D.; MacPhee, Allan A. Salmen Family Hypertension Research Laboratory,

Ochsner Medical Institutions New Orleans, LA 70121 **Angiotensin binding affinity and capacity in the midbrain area of spontaneously hypertensive and normotensive rats.** Brain Research (Amsterdam). 154(1):178-181, 1978.

The concentrations and affinity of angiotensin II (A-II) receptors in the hypothalamus, thalamus, septal, midbrain (HTSM) area of spontaneously hypertensive (SHR) and normotensive Wistar-Kyoto control rats were determined over a broad age range. Despite a significant reduction in HTSM receptor sites for A-II with age, no differences in receptor affinity or concentration were found between strains at any age. Results suggest that the well documented differences in pressure at any age between the two strains of rats do not result from differences in the affinity or concentration of their A-II receptors in the HTSM area of the brain. 14 references.

002871 Collard, K. J. Department of Physiology, University College, P.O. Box 78, Cardiff CF1 1XL, Wales. **The effect of lithium on the increase in forbrain 5-hydroxyindoleacetic acid produced by raphe stimulation.** British Journal of Pharmacology (London). 62(1):137-142, 1978.

The change in forebrain 5-hydroxindoleacetic acid (5-HIAA) concentration induced by raphe stimulation was studied in 36 male Albino Wistar rats treated with lithium or 0.9% w/v saline solution for 10 days. Raphe stimulation increased the forebrain concentration of 5-HIAA in both groups of animals. Chlorimipramine abolished this effect in the control group, but not in the lithium group. The inhibition of 5-hydroxytryptamine (5-HT) uptake by chlorimipramine was not affected by pretreatment with lithium or by the addition of lithium to synaptosomal suspensions. in vitro. It is suggested that the production of 5-HIAA following raphe stimulation in lithium-treated animals is derived from the metabolism of 5-HT which remains within the intracellular environment. The consequence of this in relation to transmitter release is discussed. 24 references. (Author abstract)

002872 Consolo, Silvana; Ladinsky, Herbert; Samanin, Rosario; Bianchi, Serenella; Ghezzi, Daniela. Instituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62, I-20157 Milan, Italy **Supersensitivity of the cholinergic response to apomorphine in the striatum following denervation or disuse supersensitivity of dopaminergic receptors in the rat.** Brain Research (Amsterdam). 155(1):45-54, 1978.

Cholinergic response to apomorphine in the striatum is related to dopaminergic receptors in female Charles River and Italia rats in a study in which unilateral lesions of the nigromeostriatal and mesolimbic dopaminergic projections are induced by infusion of 6 hydroxydopamine. At 9 days following the lesion dopamine was depleted by 90% in the striatum and 85% in the region containing the nucleus accumbens septi and tuberculum olfactorium of the ipsilateral side without affecting noradrenaline contents. A denervation supersensitivity response developed starting at two days postlesion and cholinergic sensitivity to apomorphine tripled by the end of 30 days. The data demonstrate that supersensitivity of the cholinergic response to apomorphine in the striatum accompanies denervation or disuse supersensitivity of dopaminergic receptors. The results can be interpreted as supporting inhibitory dopaminergic regulation of striatal cholinergic interneurons. 34 references. (Author abstract modified)

002873 Conway, E. L.; Jarrott, B.; Louis, W. J. University of Melbourne, Clinical Pharmacology and Therapeutics Unit, Austin Hospital, Heidelberg 3084, Victoria, Australia **Effect of alpha-methyldopa on dopaminergic transmission in the corpus striatum.** Neuropharmacology (Oxford). 17(6):355-361, 1978.

The effect of alpha-methyldopa in treatment of hypertension is investigated. Administration of 200mg/kg alpha-methyldopa (AMD) caused a decline in dopamine and a rise in alpha-methyldopamine (AMDA) levels in the corpus striatum which were maximal between 4 to 6 hours after injection. Subcellular fractionation of the striatum 4 hours after AMD administration demonstrated that AMDA had accumulated within synaptosomes in approximately equal quantities to dopamine and that the subcellular distribution of the two amines was similar. Calcium dependent release of both dopamine and AMDA could be stimulated by exposing the synaptosomes to 60mmol/liter potassium 10n. AMDA was substantially less potent than dopamine in stimulating the dopamine sensitive adenyl cyclase in striatal homogenates. At concentrations higher than those normally present in the brain following AMD administration, AMDA did not inhibit the stimulation of adenyl cyclase by dopamine. Results indicate that AMDA can act as a false transmitter in the corpus striatum, thereby impairing dopaminergic transmission. 34 references. (Author abstract)

002874 Cook, M. A.; Hamilton, J. T.; Okwuasaba, F. K. Department of Pharmacology, Faculty of Medicine, University of Western Ontario, London, Ontario Canada N6A 5C1 **Coenzyme A is a purine nucleotide modulator of acetylcholine output.** Nature (London). 271(5674):768-771, 1978.

The presynaptic inhibitory effects of coenzyme-A (CoA) and its analogues on acetylcholine release were investigated. These effects on the mechanical activity of electrically stimulated guinea-pig ileum were compared with those of the nucleotide ATP, AMP, noradrenaline, pantothenic acid, and beta-mercaptoethylamine. Additionally, the effects of CoA and the other purine nucleotide agonists were studied on the resting and stimulated release of exogenous acetylcholine (ACh) from Auerbach's plexus. Exogenous ATP as well as CoA and its analogues inhibits the release of ACh from guinea-pig ileum. It is suggested that CoA released from cholinergic nerve terminals may function as the modulator of ACh release. 22 references.

002875 Cotter, Gregory W.;Palmer, Gene C.; Palmer, S. Jo; Manian, Albert A. Department of Pharmacology, University of South Alabama, College of Medicine, Mobil, AL 36688 **Modification of adenylate cyclase systems in mouse cerebral cortex by chlorpromazine and respective 7-hydroxy analogs.** Communications in Psychopharmacology. 2(1):51-58, 1978.

Experiments were carried out in the mouse cerebral cortex to evaluate the ability of chlorpromazine (CPZ) and some of its 7-hydroxy analogs to modify the activation of adenylate cyclase by different agents, specifically norepinephrine (NF), dopamine (DA), KCL, ouabain and adenosine. In incubated tissue slices sinsitive to NF and tissue homogenates sensitive to NF and DA. adenylate cyclase was potently inhibited by CPZ and 7-hydroxy-chlorpromazine (7-OH-CPZ), while the methiodide and glucuronide of the hydroxylated compound acted similarly but to a considerably lesser extent. The action of adenosine on cyclic AMP accumulation was not influenced by either CPZ or its 7-hydroxy derivatives. Similarly, the stimulatory actions of the depolarizing agents, KCl and ouabain, were only antagonized by the highest concentrations of CPZ and 7-OH-CPZ respectively. The results indicate that the actions of neuroleptic drugs on central adenylate cyclase systems are manifested toward an antagonism of the catecholamine sensitive receptor moiety of the enzyme. 20 references. (Author abstract)

002876 Craves, Frederick B.; Loh, Horace H.; Meyerhoff, James L. Department of Pharmacology, University of California, San Francisco, CA 94143 **The effect of morphine tolerance and dependence on cell free protein synthesis.** Journal of Neurochemistry. 31(5):1309-1316, 1978.

Addition of exogenous morphine to a cell free protein synthetic system isolated from chronically morphinized, placebo treated, or naive male Swiss-Webster mouse brain had no effect on the relative synthetic capacity of the system. Morphine also failed to alter the response to a synthetic messenger ribonucleic acid, polyuridylic acid. However, both the polyribosomes and pH5 factors isolated from chronically morphinized mouse brain were more effective im promoting amino acid incorporation into protein relative to the corresponding fractions from placebo treated mice. Acrylamide gel electrophoresis of the proteins in the incubation mixture showed the increased amino acid incorporation was the result of a general quantitative increase in the specific activity of all the proteins synthesized by the cell free system. 39 references. (Author abstract)

002877 Creese, Ian; Snyder, Solomon H. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Dopamine receptor binding of 3H-ADTN (2-amino-6,7-dihydroxy-1,2,3,4,-tetrahydronaphthalene) regulated by guanyl nucleotides.** European Journal of Pharmacology (Amsterdam). 50(4):459-461, 1978.

Specific labeling of dopamine (DA) receptors with tritiated 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (3H-ADTN) was demonstrated in rat striatum. Scatchard analysis showed two components of binding with apparent dissociation constants of 6nM and 45nM and binding capacities of 15 and 35pmoles/g wet weight. Drug specificity of 3H-ADTN binding fulfilled characteristics expected of DA receptors and resembled the binding of the DA agonist 3H-apomorphine. Manganese significantly increased specific binding in a concentration dependent fashion, whereas calcium and magnesium were much less effective. Studies with guanyl nucleotides indicated that a component of 3H-ADTN binding may be associated with the DA sensitive adenylate cyclase. 5 references.

002878 Curzon, G.; Fernando, J. C. R.; Marsden, C. A. Dept. of Neurochemistry, Institute of Neurology, 33 John's Mews, London WC1N 2NS, England **5-Hydroxytryptamine: the effects of impaired synthesis on its metabolism and release in rat.** British Journal of Pharmacology (London). 63(4):627-634, 1978.

The effects of impaired 5-hydroxytryptamine (5-HT) synthesis on its metabolism and release were investigated in male Sprague-Dawley rats. Control rats given L-tryptophan showed a smaller increase of brain 5-HT than its metabolite 5-hydroxyindoleacetic acid (5-HIAA). However, when brain 5-HT concentrations were depleted by 40-50% after treatment with the synthesis inhibitor p-chlorophenylalanine (PCPA) L-tryptophan caused a considerable increase in 5-HT but no change in 5-HIAA. Electrical stimulation of the median raphe nucleus of control rats significantly increased 5-HIAA in the hypothalamus, hippocampus, and striatum. However, stimulation of PCPA pretreated animals did not significantly increase 5-HIAA either 24 hours or 72 hours after administration of the drug. Results suggest that newly synthesized 5-HT is less rapidly metabolized in rats with low brain 5-HT. The possible reasons for this and the relevance of the results to the use of L-tryptophan in the treatment of depressive illness are discussed. 28 references. (Author abstract modified)

002879 Dahlof, Lars-Gosta; Hard, Ernest; Larsson, Knut. Unit of Psychobiology, Department of Psychology, University of Goteborg, Fack, S-400 20 Goteborg, Sweden **Sexual differentiation of offspring of mothers treated with cortisone during pregnancy.** Physiology & Behavior. 21(4):673-674, 1978.

Treatment of pregnant Wistar rats with hydrocortisone (1.5or 3.0mg) from day 14 after conception until birth resulted in shortened anogenital distance and reduced testis weight in male offspring. No changes were found in anogenital distance in female offspring. It is concluded that corticosteroids, like stress, during pregnancy causes demasculinization of the male offspring. 16 references. (Author abstract)

002880 Dailey, J. W. Department of Pharmacology and Therapeutics, Louisiana State University, School of Medicine, P.O. Box 33932, Shreveport, LA 71130 **Effects of maternal chlorpromazine on offspring nervous system development.** Neuropharmacology (Oxford). 17(8):583-587, 1978.

Administration of chlorpromazine (7mg/kg/day) to Sprague-Dawley rat dams from day 8 of pregnancy until pups were weaned produced small but statistically significant decreases in litter size and birth weight. Weight differences were no longer apparent at time of weaning, however. The offspring of chlorpromazine treated dams were less able to maintain body temperature in response to restrained cold stress, determined when they were 60-65 days of age. These pups incorporated significantly less C14 from tyrosine into heart norepinephrine during acute cold exposure, although no differences were evident when the animals were not exposed to cold stress. Treated offspring also failed to show the increase in superior cervical ganglion tyrosine hydroxylase activity seen in offspring of control dams after 48 hours of cold exposure. Results suggest that maternal administration of chlorpromazine produces a permanent alteration in the ability of offspring to response to cold stress and that this deficit is related to an alteration in nervous system development. 25 references. (Author abstract modified)

002881 Dalterio, S.; Bartke, A.; Roberson, C.; Watson, D.; Burstein, S. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Direct and pituitary-mediated effects of delta9-THC and cannabinol on the testis.** Pharmacology Biochemistry and Behavior. 8(6):673-678, 1978.

In an effort to determine a mechanism of action of delta9-tetrahydrocannabinol (THC) and cannabinol (CBN) on the accumulation of testosterone (T) and progesterone (P), experiments were conducted with mouse testes. In testes incubated with human chorionic gonadotropin (hCG), addition of THC resulted in a significant inhibition in the accumulation of T and P. The inhibition of T production in this in vitro system by THC was dependent upon the presences of hCG in the medium, suggesting that THC may interfere with gonadotropin stimulation of testicular steroidogenesis. In contrast, suppression of T secretion by CBN also occurred in the absence of hCG. In the in vivo studies, administration of a single oral dose of THC to adult male mice resulted in a reduction in plasma T, luteinizing hormone (LH) and follicle stimulating hormone levels, as well as an increase in the concentration of esterified cholesterol in the testis. In contrast, a single dose of CBN produced no significant changes in either plasma T or gonadotropin levels. Treatment with THC, but not with CBN, resulted in a pronounced reduction in the level of copulatory activity in adult male mice. It appears that the THC-induced reduction in plasma T levels observed in vivo is due to an inhibition of pituitary LH release, and to a direct effect on the testicular responsiveness to LH stimulation. The reduction in copulatory behavior observed after acute exposure to THC may be secondary to a reduction in peripheral T concentration. The results suggest a possible mechanism for the action of THC testes function; however, the action of cannabinoids on the pituitary gonadal axis is not clear. 45 references. (Author abstract modified)

002882 Davie, John; Tongroach, Parich. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Neuropharmacological studies on the nigro-striatal and raphe-**

striatal system in the rat. European Journal of Pharmacology (Amsterdam). 51(2):91-100, 1978.

The responses of single neostriatal neurons to substantia nigra (SN) and dorsal raphe nucleus (DRN) stimulation and iontophoretic administration of several drugs were studied in urethane anesthetized rats. Stimulation of the SN evoked excitation followed by inhibition in striatal neurons. In some cells, only inhibition of firing was evoked, indicating that there may be separate nigrostriatal inhibitory and excitatory pathways. DRN stimulation evoked mainly inhibition of striatal cell firing. The activity of most neurons responding to SN and DRN stimulation was depressed by iontophoretically applied dopamine (DA), 5-hydroxytryptamine (5-HT), and gamma-aminobutyric acid (GABA), and was increased by acetylcholine. Alpha-flupenthixol reduced responses to DA and 5-HT and inhibition evoked by SN and DRN stimulation. Bicuculline methochloride reduced only responses to GABA. Methysergide selectively reduced responses to 5-HT and also reduced DRN but not SN evoked inhibition. It is concluded that the SN evoked inhibition was probably mediated by DA, while the DRN evoked inhibition was mediated by 5-HT. 40 references. (Author abstract modified)

002883 Davies, J.; Dray, A. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Pharmacological and electrophysiological studies of morphine and enkephalin on rat supraspinal neurones and cat spinal neurones.** British Journal of Pharmacology (London). 63(1):87-96, 1978.

The effects of electrophoretically administered morphine, methionine, and leucine enkephalin on supraspinal neurons in the cortex and brainstem of rats anesthetized with urethane and on spinal Renshaw cells and dorsal horn interneurons in cats anesthetized with pentobarbitone were studied. The majority of Renshaw cells and cortical and brainstem neurons were excited by all three compounds, although some supraspinal neurons were depressed. Naloxone reversibly antagonized both excitatory and depressant actions of morphine and enkephalin. Naloxone also antagonized excitation induced by acetylcholine but not by amino acids. Neither morphine nor the enkephalins had any naloxone reversible action on dorsal horn neurons when ejected from conventional multibarrelled electrodes. However, morphine but not enkephalin administered into the substantia gelatinosa region of the spinal cord selectively reduced responses to noxious stimuli of neurons in deeper laminae; this action was reversed by naloxone. Intravenous morphine also antagonized responses of dorsal horn neurons to noxious stimuli, and subsequent intravenous naloxone reversed this effect. 58 references. (Author abstract modified)

002884 Davis, A.; Roberts, P. J.; Woodruff, G. N. Pharmacology Group, School of Biochemical and Physiological Sciences, University of Southampton, Southampton SO9 3TU, England **The uptake and release of (3H)-2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (ADTN) by striatal nerve terminals.** British Journal of Pharmacology (London). 63(1):183-190, 1978.

The uptake and release of (G-3H)-2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronapthalene (ADTN) by crude striatal synaptosomes from female Wistar rats were examined. Uptake was rapid and temperature dependent and could be suppressed by a variety of metabolic inhibitors. The Michaelis-Menten kinetics indicated the presence of two distinct transport systems in the striatum with much higher capacity than those of the cerebellum. Uptake of (3H)ADTN was strongly inhibited by dopamine, benztropine, and nomifensine, but only weakly inhibited by imipramine and amphetamine. Accumulated (3H)-ADTN could be released from striatal slices by elevated postassium and by the addition of the calcium ionophore A23187. The most potent releaser of (3H)-ADTN was ()-amphetamine; this effect occurred at concentrations inactive against ADTN uptake. The neuroleptic cis-flupenthixol produced, an inhibition of the spontaneous release. It is concluded that (3H)-ADTN is accumulated preferentially into areas of rat brain rich in dopamine. The release of (3H)-ADTN by potassium and a calcium ionophore raises the possibility that ADTN may act as a false transmitter in dopaminergic neurons. 26 references. (Author abstract modified)

002885 Davis, James N.; Arnett, Carroll D.; Hoyler, Elizabeth; Stalvey, Linda P.; Daly, John W.; Skolnick, Phil. Neurology Research Laboratory, Veterans Administration Hospital, Duke University Medical Center, Durham, NC 27705 **Brain alpha-adrenergic receptors: comparison of (3H)WB 4101 binding with norepinephrine-stimulated cyclic AMP accumulation in rat cerebral cortex.** Brain Research (Amsterdam). 159(1):125-135, 1978.

The ability of a series of adrenergic agents to displace the binding to brain membranes of tritiated 2-(2-(2,6-dimethoxyphenoxy) ethylaminomethyl)-1,4-benzodioxane hydrochloride (WB-4101, a potent alpha-adrenergic antagonist) was compared with the potency of these agents in stimulating or inhibiting the alpha-adrenergic component of cyclic adenosine monophosphate (AMP) accumulation in cerebral cortical slices from male Sprague-Dawley rats. The potencies of adrenergic agents (WB-4101, phentolamine, and naphazoline) in displacing (3H)WB-4101 were comparable to the potencies of these agents as inhibitors of the alpha-adrenergic component of norepinephrine (NE) stimulated cyclic AMP accumulations. Phenoxybenzamine, clonidine, chlorpromazine, and haloperidol were about 10-30 times more potent in inhibiting cyclic AMP accumulation than in displacing (3H)WB-4101 binding. The potency of classical alpha-adrenergic agonists (epinephrine, NE, and methoxamine) in displacing WB-4101 correlated with the ability of these agonists to increase cycle AMP levels. Results indicate that WB-4101 may bind to the membrane receptor sites mediating the alpha-adrenergic accumulation of cyclic AMP in rat cerebral cortex. 37 references. (Author abstract modified)

002886 Dawson, Glyn; Kernes, Stewart M. Dept. of Pediatrics, Joseph P. Kennedy Jr. Mental Retardation Research Center, University of Chicago, Chicago, IL 60637 **Induction of sulfogalactosylceramide (sulfatide) synthesis by hydrocortisone (cortisol) in mouse G-26 oligodendroglioma cell strains.** Journal of Neurochemistry (Oxford). 31(4):1091-1094, 1978.

The effect of corticosteroids on glycosphingolipid biosynthesis in cultured cells of nervous system origin, mouse G-26 oligodendroglial cell strains, was investigated. When H235SO4 labeling for 24 hours was carried out in the presence of increasing concentrations of hydrocortisone (cortisol) more than a two fold stimulation of sulfogalactosylceramide synthesis was observed with maximum induction occurring at 5 x 10-6M hydrocortisone. Maximum six fold enhancement of synthesis at 5 x 10-6M was observed after 24 to 30 hours incubation. It is concluded that the enzyme appears to be associated with oligodendroglial cells and its induction may be an integral part of the process of myelination. 19 references.

002887 de Kloet, E. Ronald; Burbach, Peter. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, Utrecht, The Netherlands **Selective purification of a single population of glucocorticoid receptors from rat brain.** Journal of Neurochemistry (Oxford). 30(6):1505-1507. 1978.

The fractionation and purification of the specific glucocorticoid binding macromolecules using affinity chromatography via deoxycorticosterone hemi-succinate covalently coupled to BSA

Sepharose 4B to achieve a selective purification of one of the two distinct receptor populations is described. A 200 fold purification of glucocorticoid receptors from rat brain was achieved with 21% recovery using this method. Subsequent chromatography of the affinity column eluate via a DE 52 anion exchanger revealed that this purification concerned selectively one of the two glucocorticoid receptor systems in rat brain. 18 references. (Author abstract modified)

002888 de la Ilyas, M. S.; Iglesia, F. A.; Feuer, G. Department of Clinical Biochemistry, University of Toronto, Toronto, Ontario M5G 1L5, Canada **The effect of phenobarbital and carbon tetrachloride on fatty acid content and composition of phospholipids from the endoplasmic reticulum of rat liver.** Toxicology and Applied Pharmacology. 44(3):491-504, 1978.

The fatty acid content and composition of hepatic microsomes of separated smooth and rough components and of isolated phosphatidycholine and phosphatidylethanolamine fractions were studied in male Wistar rats treated with phenobarbital or carbon tetrachloride. Both test compounds significantly altered the fatty acid composition of the endoplasmic reticulum. The total amount was raised by phenobarbital and reduced by carbon tetrachloride. Phenobarbital enhanced palmitic, stearic, arachidic, palmitoleic, linoleic, eicosenoic, eicosadienoic, eicosapentenoic, docosatrienoic, and docosahexenoic acids. Similar findings in rough and smooth microsomes and in microsomal phosphatidylcholine and phosphatidylethanolamine fractions are discussed. The saturated/unsaturated fatty acids ratio was reduced by phenobarbital and increased by carbon tetrachloride, and thus may indicate a selective difference between an inducer and hepatotoxin of fatty acid synthesis of the hepatic endoplasmic reticulum. 37 references. (Author abstract modified)

002889 De Vries, Gerald W.; Friedman, Alexander H. Department of Pharmacology, Loyola University Stritch School of Medicine, Maywood, IL 60153 **GABA, picrotoxin and retinal sensitivity.** Brain Research (Amsterdam). 148(2):530-535, 1978.

The effects of gamma-aminobutyric acid (GABA) and the GABA antagonist picrotoxin on retinal sensitivity of the frog (Rana pipiens) were examined. Exogenous GABA applied to the dark adapted retina depressed the maximum response obtainable in the dark, without significantly altering the neural adaptation mechanism activated by weak background light. Picrotoxin, presumably through its antagonism of endogenous GABA, enhanced the response of the dark adapted retina and quantitatively altered the neural mechanisms involved in retinal adaptation to weak background light. Administration of GABA or picrotoxin had no effect on aspartate isolated receptor potentials, suggesting that the effect of these agents on retinal sensitivity involves mechanisms operating proximal to photoreceptors. Administration of dopamine, acetylcholine, or acetylcholine plus physostigmine had no effect on retinal response, suggesting that control of retinal sensitivity is specifically related to a GABA mediated mechanism. 14 references.

002890 Deakin, J. F. W.; Dostrovsky, J. O. National Institute for Medical Research, Mill Hill, London NW7 1AA, England **Involvement of the periaqueductal grey matter and spinal 5-hydroxytryptaminergic pathways in morphine analgesia: effects of lesions and 5-hydroxytryptamine depletion.** British Journal of Pharmacology (London). 63(1):159-165, 1978.

The central nervous system mechanisms of morphine analgesia were examined. The analgesia produced by intraperitoneal injection of morphine (10 and 20mg/kg) was substantially reduced in male Sprague-Dawley rats given electrolytic lesions of the periaqueductal gray matter (PAG); baseline pain thresholds were unaffected by the lesions. The extent of histologically determined damage to the dorsal raphe nucleus and the resulting decrease in striatal 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) concentrations did not correlate with the reduction in morphine analgesia produced by the lesion. Microinjections of 5,6-dihydroxytryptamine into the dorsal raphe nucleus produced a similar fall in 5-HIAA levels but had no effect on morphine analgesia. Selective destruction of the periventricular catecholamine system produced by microinjection of 6-hydroxydopamine caused a slight decrease in morphine analgesia, suggesting that catecholamines may be involved in the action of morphine in the PAG. Lesions of the spinal cord 5-HT pathways induced by 5,7-dihydroxytryptamine reduced cord 5-HT concentration by 70% and markedly attenuated morphine analgesia. Results suggest that the PAG is a major site of action in opiate analgesia and that spinal 5-HT pathways are involved in the mediation of opiate analgesic effects. 29 references. (Author abstract modified)

002891 DeBold, Joseph F. Department of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **Modification of nuclear retention of (3H)estradiol by cells of the hypothalamus as a function of early hormone experience.** Brain Research (Amsterdam). 159(2):416-420, 1978.

The nuclear accumulation and retention of estradiol by cells of the hypothalamus/preoptic area, mesencephalon, and cerebral cortex was studied in male hamsters and in female hamsters injected with varying amounts of testosterone propionate (TP) 24 hours after birth. The effect of early androgen exposure on estrogen retention was not significant in the mesencephalic and cortical samples. Hypothalamic nuclear retention of estradiol in males and in females treated with 500mcg TP treated females was significantly impaired, compared to that of controls and 5mcg TP treated females. These results indicate that the retention of estradiol in hypothalamic nuclei is at least partially a function of neonatal exposure to androgen. Findings are discussed in relation to previous studies of reduced behavioral sensitivity to estrogen associated with early exposure to androgen. 38 references.

002892 DeFeudis, Francis V. Centre de Neurochimie, 11, rue Humann, F-67085 Strasbourg Cedex, France **Vertebrate GABA receptors.** Neurochemical Research. 3(3):263-280, 1978.

Physiological and pharmacological studies of gamma-aminobutyric acid (GABA) receptors in vertebrates are reviewed. Experiments in vivo and with tissue cultures have revealed that synaptic GABA receptors exist in the vertebrate CNS. The GABA antagonist bicuculline can be used to detect synaptic GABA receptors in both the presence and absence of sodium ion, even though GABA binding to cerebral subcellular fractions occurs mainly to uptake receptors in the presence of sodium ion. Further studies on GABA receptors should reveal the roles that GABA mediated mechanisms play in the regulation of animal behavior and in certain human neurologic and psychiatric disorders. 92 references. (Author abstract modified)

002893 Dial, Elizabeth J.; Clarke, David E. Department of Pharmacology, College of Pharmacy, University of Houston, Houston, TX 77004 **Phenylethylamine -- deamination by multiple types of monoamine oxidase.** Biochemical Pharmacology (Oxford). 27(19):2374-2375, 1978.

The deamination of 2-phenylethylamine (PEA) in liver, ventricle, and vasa deferentia homogenates from male Wistar rats was examined. High concentrations of clorgyline were required to inhibit PEA deamination in the rat liver, even though considerable type A monoamine oxidase (MAO) activity exists in this organ. PEA deamination proceeded through both type A and type B MAO in the vasa deferentia. In the ventricles, PEA was

deaminated by type A MAO. Results indicate that PEA can serve as a type A substrate, a dual substrate, or a type B substrate, depending on the organ examined. Consequently, the deamination of PEA can no longer be taken as presumptive evidence of type B activity in whole cell homogenates in the absence of additional proof. 23 references.

002894 Dibner, Mark D.; Black, Ira B. Laboratory of Developmental Neurology, Cornell University Medical College, 515 East 71st Street, New York, NY 10021 **Biochemical and morphological effects of testosterone treatment on developing sympathetic neurons.** Journal of Neurochemistry (Oxford). 30(6):1479-1483, 1978.

Neonatal rats were treated with testosterone propionate (TP) or isoproterenol (ISO) to determine whether: 1) increases in salivary gland mass are associated with alteration of developing sympathetic neurons, and 2) whether effects on neuron growth are secondary to altered target mass itself or to increases in salivary growth factors. TP treatment is known to result in salivary tubule hypertrophy and elevated nerve growth factor (NGF) content whereas ISO treatment results in acinar hypertrophy and no known alteration in NGF. TP treatment increased submaxillary gland weight as well as tyrosine hydroxylase (T-OH) activity, adrenergic neuron numbers and total protein in the innervating superior cervical ganglion (SCG). Unilateral sialectomy prevented the increase in T-OH activity in the SCG, suggesting that the salivary glands were necessary for this effect. T-OH activity and total protein were elevated in the distant sixth lumbar sympathetic ganglion after TP treatment, suggesting that sympathetic development as a whole was affected and that humoral factors may be involved. Salivary gland weight was also elevated following ISO administration, but T-OH activity in the SGG was not affected. These observations suggest that TP treatment increases T-OH activity and sympathetic neuron numbers by alteration of specific salivary humoral growth factor(s). 29 references. (Author abstract)

002895 Dillier, N.; Laszlo, J.; Muller, B.; Koella, W. P.; Olpe, H.-R. Biological Research Laboratories, CIBA-Geigy Ltd., CH-4002 Basel, Switzerland **Activation of an ihhibitory noradrenergic pathway projecting from the locus coeruleus to the cingulate cortex of the rat.** Brain Research (Amsterdam). 154(1):61-68, 1978.

Repetitive stimulation of the locus coeruleus evoked strong inhibition of the firing rate of about 50% of cells of the cingulate cortex of Sprague-Dawley rats. Forty percent of the cells were not affected and 9% were excited by stimulation of the locus coeruleus. Pretreatment with reserpine and alpha-methyl-p-tyrosine drastically reduced the percentage of cells inhibited by locus coeruleus stimulation. The cells inhibited in response to stimulation of the locus coeruleus, as well as those not inhibited, were depressed by microiontophoretically applied norepinephrine (NE). This inhibitory action of NE was observed in rats anesthetized with urethane, chloral hydrate, or Nembutal. The transsynaptically elicited, as well as the NE elicited, depression of the cells' discharge was antagonized by the microiontophoretically applied beta-receptor blocking drug MJ-1999. Results suggest that the inhibitory action on cingulate cortical cells of locus coeruleus stimulation is mediated by the dorsal ascending noradrenergic pathway. 14 references. (Author abstract)

002896 Doherty, John D.; Roth, Robert H. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Metabolism of gamma-hydroxy-(1-14C) butyrate by rat brain: relationship to the Krebs cycle and metabolic compartmentation of amino acids.** Journal of Neurochemistry (Oxford). 30(6):1305-1309, 1978.

A study of the enzyme in the rat brain involved in the metabolism of gamma-hydroxy-(1-14C) butyrate acid (GHB) was conducted in order to assess the possible role endogenous GHB may play in CNS function. Ninhydrin decarboxylation experiments were carried out on the labelled amino acids produced following intraventricualr injection of either GHB or (1-14C) succinate. The loss of isotope was similar for both substances. The 1-14C GHB metabolites lost 75% of the label and the 1-14C succinate metabolites lost 68%. This observation gives support to the hypothesis that the rat brain has the enzymatic capacity to metabolize 1-14C GHB to succinate and to amino acids that have the isotope in the carboxylic acid group adjacent to the alpha-amino group. These results also indicate that the label from 1-14C GHB does not enter the Krebs cycle as acetate. The specific activity ratio of radiolabelled glutamine to glutamic acid was determined in order to evaluate which of the two major metabolic compartments preferentially metabolize GHB. These results suggest that the compartment thought to be associated with glial cells and synaptosomal structures is largely responsible for the metabolism of GHB. Metabolism as it might relate to the neuropharmacological action of GHB is discussed. 23 references. (Author abstract modified)

002897 Donaldson, I. M. L.; Long, A. C.; Tasker, T. C. G. University Laboratory of Physiology, Parks Road, Oxford OX1 3PT, England **Suppression by nitrous oxide of visual responses in the cerebellar vermis and superior colliculus of cats anaesthetized with chloralose.** Brain Research (Amsterdam). 148(2):526-529, 1978.

The effect of nitrous oxide on the visual responses in the cerebellar vermis and superior colliculus of cats anesthetized with chloralose was examined. Concentrations of nitrous oxide as low as 50% were associated with great reduction or abolition of visual responses of units in the cerebellar vermis, while the spontaneous firing rate of these units was barely affected by nitrous oxide. Nitrous oxide also reduced responses of units in the superior colliculus, with the magnitude of the effect varying from complete abolition of all responses to visual stimulation, to minimal reduction of the response amplitude; no effect on spontaneous activity of these units was observed after nitrous oxide. It is concluded that nitrous oxide in combination with chloralose exerts a specific depressant effect on the responses of some visual units, without significantly affecting their spontaneous activity. Consequently, nitrous oxide should be avoided in visual experiments on the collicular or cerebellar pathway in animals under chloralose anesthesia. 16 references.

002898 Dunn, Adrian J.; Gildersleeve, Nancy B.; Gray, Harry E. Dept. of Neuroscience, University of Florida College of Medicine, Gainesville, FL 32610 **Mouse brain tyrosine hydroxylase and glutamic acid decarboxylase following treatment with adrenocorticotrophic hormone, vasopressin or corticosterone.** Journal of Neurochemistry (Oxford). 31(4):977-982, 1978.

The activities of tyrosine hydroxylase (TH) and glutamix acid decarboxylase (GAD) from several mouse brain regions were assayed following repeated administration of adrenocorticotrophic hormone (ACTH), lysine vasopressin (LVP) or corticosterone. Although similar treatments with ACTH have been shown to result in changes of catecholamine turnover and GABA content, no changes in the activity of either TH or GAD were observed in any brain region. Likewise LVP had no effect on either enzyme. Since the assays for TH were performed with concentrations of tyrosine and tetrahydrobiopterin cofactor below their respective Michaelis constants, this suggests that the changes of catecholamine turnover are not mediated by changes of TH activity. Twice daily corticosterone administration for four days increased TH activity in the hypo-

thalamus but not in any other brain region. 26 references. (Author abstract)

002899 Edgar, D. H; Thoenen, H. Department of Pharmacology, Biocenter of the University, Basel, Switzerland **Selective enzyme induction in a nerve growth factor-responsive pheochromocytoma cell line (PC 12).** Brain Research (Amsterdam). 154(1):186-190, 1978.

The selective induction of enzymes necessary for transmitter synthesis in pheochromocytoma cell line PC12 was demonstrated and compared with that observed in other neural crest derivatives. Nerve growth factor (NGF) induced no significant change in tyrosine hydroxylase (TH) specific activity when compared with untreated control cultures of equal cell density over a 70 hour incubation period. NGF increased the specific activity of choline acetyltransferase (CAT) at low density, but induced no significant change at high cell density. Treatment of the cells with dexamethasone inhibited any increase in CAT activity due to NGF or cell density and increased TH levels up to 5 fold. It is concluded that the PC12 cells have functional NGF receptors but are unable to respond to NGF by induction of TH. 19 references.

002900 Edwards, David J.; Malsbury, Charles W. Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **Characteristics of monoamine oxidases in brain and other organs of the golden hamster.** Biochemical Pharmacology (Oxford). 27(6):959-963, 1978.

The activities of monoamine oxidase (MAO) were measured with the type-A substrate, serotonin, and the type-B substrate, phenylethylamine (PE), in brain, heart, kidney, lung, liver, and spleen of male golden hamsters, albino rabbits, and Sprague-Dawley rats. The relative activities measured with the two substrates varied markedly among different organs of the same species and among the same organ of different species. The rabbit had the lowest A/B ratio for each of the organs examined. The A/B ratios in the hamster were comparable to those of the rat for each of the organs, except for a higher ratio in the brain and a lower ratio in the heart. The activity measured with PE for hamster brains was only 7 and 8% of the corresponding activity in the brain of rat and rabbit, respectively. Studies using the selective inhibitors, clorgyline and deprenyl, in combination with selective substrates, indicated that the small amount of activity in hamster brain toward substrate PE was due to MAO-B rather than MAO-A. The advantages of this method for the detection of multiple forms of MAO, particularly when the amount of one form is very small as compared with the other are discussed. 12 references. (Author abstract modified)

002901 Evans, R. H.; Francis, A. A.; Watkins, J. C. Department of Pharmacology, Medical School, University of Bristol, Bristol BS8 1TD, England **Mg2-like selective antagonism of excitatory amino acid-induced responses by alpha,epsilon-diaminopimelic acid, D-alpha-aminoadipate and HA-966 in isolated spinal cord of frog and immature rat.** Brain Research (Amsterdam). 148(2):536-542, 1978.

The effects on isolated hemisected frog and immature rat spinal cords of two longer chain analogues of glutamic and aspartic acids, D-alpha-aminoadipic acid (AAA) and alpha,epsilon-diaminopimelic acid (DPA), were examined. DPA (0.5mM) reduced ventral root potentials evoked by stimulation of the corresponding dorsal root (DR-DVPs) by about 50% and reduced dorsal root potentials evoked by the same stimulus and recorded from an adjacent dorsal root (DR-DRPs) by about 20%. DPA abolished spontaneous activity and responses to N-methyl-D-aspartate, reduced responses to L-aspartate by about 50% and to L-glutamate by about 30%, and selectively antagonized excitatory responses induced by amino acids. AAA produced a similar range of effects on spontaneous activity, DR-VRPs, DR-DRPs, and amino acid-induced root potentials. HA-966 (3-amino-1-hydroxy-2-pyrrolidone), magnesium, and L-glutamic acid diethyl ester showed a similar pattern of depressant actions to those seen with DPA or AAA. Findings suggest that the depression of spontaneous activity and of electrically evoked root potentials by these agents is the result of a specific antagonism of amino acid mediated synaptic excitation in the spinal cord. 16 references.

002902 Fabian, Ina; Aronson, Moshe. Department of Cell Biology and Histology, Sackler School of Medicine, Tel-Aviv University, Ramart Aviv, Israel **Monoamine oxidase activity of macrophages at rest and during phagocytosis.** Biochemical Pharmacology. 27(15):1909-1911, 1978.

Monoamine oxidase (MAO) activity was investigated in mouse macrophages at rest and during phagocytosis. Strong deamination of 5-hydroxytryptamine and tyramine and marginal deamination of benzylamine indicated the presence of type A MAO activity and traces of type B MAO activity in mouse macrophages. Significant inhibition of MAO activity occurred in the prescence of the specific inhibitors clorgyline and deprenyl. MAO A activity was considerably depressed in phagocytizing cells. 16 references. (Author abstract modified)

002903 Fang, Victor S.; Ho, Beng T.; Meltzer, Herbert Y. Department of Medicine, University of Chicago, Chicago, IL 60637 **Effect of 6-methoxy-tetrahydro-beta-carboline on serum prolactin levels of male rats.** Communications in Psychopharmacology. 2(1):59-63, 1978.

The effect, of 6-methoxy-tetrahydro-beta-carbooine (MTBC), a sterically hindered analog of serotonin, on serum prolactin levels in male Spraue- Dowley rats were examined. MTBC stimulated rat prolactin release in a dose related manner. The onset of the hyperprolactinemic effect was rapid and of short duration. Its effect upon serum prolactin was blocked by methysergide, a serotonin receptor blocker, and was potentiated by pretreatment -- with p-chlorophenylalanine, an inhibitor of serotonin synthesis, suggesting its action could be the result of a direct serotonergic effect on the brain. 29 references. (Author abstract)

002904 Farska, I.; Krulik, R. Psychiatric Clinic, Ke Karlovu 11, 1200 Prague 2, Czechoslovakia **Effects of psychotropic drugs on deaminase in CNS.** Activitas Nervosa Superior (Praha). 29(1):58-59, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the effects of psychotropic drugs on deaminase in the CNS are described. The effects of phenothiazines, tricyclic antidepressants, benzodiazepines, psychostimulants, and monovalent cations on the activity of adenylate deaminase, adenosine deaminase, and guanine deaminase in homogenates of rat cortex were investigated. The stimulation of deamination processes by chlorpromazine, amitriptyline, and chlordiazepoxide is discussed in terms of the possibility that a number of centrally acting compounds could stimulate the formation of some metabolites and bases that play an important part in the resynthesis of nucleotides. 5 references

002905 Feldman, R. S.; Kursat, I. University of Massachusetts, Amherst, MA 01003 **Discriminative properties of chlordiazepoxide: a new method of analysis.** Psychopharmacology (Berlin). 58(2):6, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a new method of analysis for the discriminative properties of chlordiazepoxide (CDP) was discussed. Combining CDP with the serotonin (5-HT) agonist fluoxetine (FXT) blocks the benzodiazepine cue in rats trained to discrimiante between CDP and saline on a two lever discrimination task. FXT selectively blocks the 5-HT uptake pump, depresses 5-HT turnover, and enhances postsynaptic excitation. CDP also depresses 5-HT turnover, but with the opposite effect on impulse transmission: at low doses, CDP slows 5-HT depletion induced by synthesis inhibitors without affecting synthesis, recapture, or metabolism. This suggests that CDP-induced depression of 5-HT turnover is due to reduced 5-HT release. FXT antagonism of the CDP cue suggests that the CDP cue may be a reduction of impulse transmission in 5-HT systems. The new method of data analysis is based on the calculated cumulative binomial probability that selections are due to chance. (Author abstract modified)

002906 Felix, Dominik; Schlegel, Werner. Institute for Brain Research, University of Zurich, CH-8029 Zurich, Switzerland **Angiotensin receptive neurones in the subfornical organ. Structure-activity relations.** Brain Research (Amsterdam). 149(1):107-116, 1978.

The actions of angiotensin-II and angiotensin fragments on neurones of the subfornical organ (SFO) were investigated by microiontophoresis in adult cats. Angiotensin-II-(2-8)-heptapeptide stimulated a significantly higher firing rate than did angiotensin-II. Angiotensin-II-(5-8)-tetrapeptide produced an excitatory action on single units. The actions of both the heptapeptide and the tetrapeptide were blocked by (Sar1, Ala8)-angiotensin II (P 113). In contrast, angiotensin-II-(6-8)-tripeptide failed to enhance the firing rate of the same neurones. Data indicate that angiotensin-II and some shorter chain peptide fragments directly affect neurones of the SFO. These findings support the hypothesis that the SFO is a receptor site which is available to angiotensin. 40 references. (Author abstract modified)

002907 Ferri, S.; Arrigo Reina, R.; Santagostino, A.; Scoto, G. M.; Spadaro, C. Institute of Pharmacology, Faculty of Pharmacy, University of Catania, Italy **Effects of met-enkephalin on body temperature of normal and morphine tolerant rats.** Psychopharmacology (Berlin). 58(3):227-281, 1978.

The endogenous opioid met-enkephalin intraventricularly administered to male Sprague-Dawley rats at a dose of 100mcg raised rectal temperature, while 400mcg of the pentapeptide caused a diphasic effect (hypothermia followed by hyperthermia). Met-enkephalin was ineffective when administered intraperitoneally. The effects of met-enkephalin on temperature were similar to those elicited by morphine, which may either raise or lower rat temperature, depending on the dose. More naloxone than morphine was required to antagonize thermic effects of met-enkephalin. Centrally administered met-enkephalin had no thermic effects in morphine tolerant animals. Results provide further evidence of cross tolerance between opiates and naturally occurring ligands of opiate receptors. 22 references. (Author abstract modified)

002908 Fex, Jorgen; Adams, Joe C. Laboratory of Neuro-otolaryngology, National Institute of Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD 20014 **Alpha-bungarotoxin blocks reversibly cholinergic inhibition in the cochlea.** Brain Research (Amsterdam). 159(2):440-444, 1978.

The effect of alpha-bungarotoxin (aBT) on the inhibition of sound evoked activity of the auditory nerve and the slow cochlear potential normally evoked by the crossed cochlear efferents was studied in cats. Results indicate that aBT blocked these efferent effects and also blocked the efferently caused increase in cochlear microphonics. The aBT block of these efferent effects was largely reversible. The finding that aBT functionally blocks crossed cochlear efferents indicates that these efferents are cholinergic. The reversibility of the block indicates tht these receptors are different from cholinergic receptors at other vertebrate synapses. 33 references.

002909 Fields, J. Z.; Reisine, T. D.; Yamamura, H. I. Department of Pharmacology, Chicago Medical School, 2020 W. Ogden Avenue, Chicago, IL 60612 **Loss of striatal dopaminergic receptors after intrastriatal kainic acid injection.** Life Sciences (Oxford). 23(6):569-573, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the time course of dopaminergic (DA) and muscarinic cholinergic (MCHOL) receptor alterations after kainic acid injection into the male Sprague-Dawley rat striatum is described. Histological examination showed that most striatal perikarya in the injected area were destroyed within 2 days of unilateral, intrastriatal injection of kainic acid. A progressive decrease in the DA and MCHOL receptors continued; this decrease was not due to changes in receptor affinity. By 48 days after injection, there was about 75% decrease in DA receptors and about 65% decrease in MCHOL receptors. The DA receptor loss was similar in extent to the reported loss in activity of striatal, dopamine stimulated adenylate cyclase after kainic acid lesions. The DA and MCHOL receptor loss was similar to the reported loss of neostriatal and MCHOL receptors in Huntington's Diseases. 19 references. (Author abstract modified)

002910 Fjalland, Bjarne; Boeck, Vita. Dept. of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500 Valby, Denmark **Neuroleptic blockade of the effect of various neurotransmitter substances.** Acta Pharmacologica et Toxicologica (Copenhagen). 42(3):206-211, 1978.

The antagonistic effects of six neuroleptics to the neurotransmitters acetylcholine, histamine, 5-hydroxytryptamine (5-HT), dopamine, and noradrenaline (NA) were examined in various in vivo and in vitro rat, guinea pig, and cat models. Piflutixol, a new potent thioxanthene neuroleptic, markedly antagonizes the effect of dopamine, NA, 5-HT and to some extent histamine, whereas the affinity for muscarinic receptors is rather weak. Clozapine and chlorprothixene, on the other hand, have a high affinity for muscarinic receptors and also antagonize the effect of histamine and 5-HT, whereas clozapine is a weak antagonist of NA and dopamine when compared to the effect of piflutixol. Chlorprothixene, however, exhibits a rather good antagonism of NA and dopamine. Haloperidol proved to be weak in all models when compared with the other neuroleptics examined. Flupenthixol specifically antagonized dopamine and NA, whereas fluphenazine was a more potent antagonist of dopamine than of the other transmitters. The data show that neuroleptic compounds possess very different profiles with regard to interaction with various neurotransmitter substances. It is suggested that the rather potent anti-5-HT and antihistamine effects observed for certain substances may contribute to the central effect of these drugs. 27 references. (Author abstract modified)

002911 Fonnum, F.; Walaas, I. Norwegian Defense Research Establishment, Division for Toxicology, P. O. Box 25, N-2007 Kjeller, Norway **The effect of intrahippocampal kainic acid injections and surgical lesions on neurotransmitters in hippocampus and septum.** Journal of Neurochemistry (Oxford). 31(5):1173-1181, 1978.

Local injection of kainic acid (2mcg) in rats was accompanied by destruction of intrinsic neurons in the dorsal part of the hippocampus. The lesion was accompanied by a 75% reduction in glutamate decarboxylase (GAD) activity; a 60% reduction in high affinity uptake of L-glutamate; a 40-60% reduction in endogenous levels of aspartate, glutamate, and gamma-aminobutyric acid (GABA); and no changes in the activities of choline acetyltransferase (ChAT) or aromatic amino acid decarboxylase (AAD) in the dorsal hippocampus. Unilateral destruction of neurons in the dorsal hippocampus was followed by a 20-40% reduction in the high affinity uptake of glutamate in lateral but not medial septum on both sides. There was no reduction in ChAT, GAD, or AAD activities in the lateral or medial part of the septum. Transection of fimbria and superior fornix was accompanied by a severe reductions in ChAT and AAD activity in hippocampus, in the high affinity uptake of glutamate, and in the endogenous level of glutamate in the lateral septum. Results suggest that kainic acid destroys intrinsic neurons and not afferent fibers in the hippocampus. All GABA mediated fibers in the hippocampus appear to belong to intrinsic neurons, whereas glutaminergic and aspartergic neurons belong partly to local neurons. The connection from hippocampus to the lateral septum probably uses glutamate as a transmitter. 53 references. (Author abstract modified)

002912 Fowler, Christopher J.; Callingham, Brian A. Department of Pharmacology, University of Cambridge, Hills Road, Cambridge, CB22QD, England **Substrate-selective activation of rat liver mitochondrial monoamine oxidase by oxygen.** Biochemical Pharmacology (Oxford). 27(16):1995-2000, 1978.

The activation by oxygen of monamine oxidase (MAO) activity was studied in preparations of rat liver mitochondrial membrane vesicles. Increases in MAO activity with 5-hydroxytryptamine, tyramine, beta-phenethylamine, phenethylamine, and benzylamine as substrates were uncompetitive in all cases, although the degree of activation depended upon the substrate used. It is suggested that MAO activity can be divided into two forms unrelated to MAO-A and MAO-B. These two forms, tentatively called MAO-1 and MAO-2, differ in their Michaelis constants for oxygen. Results reinforce the conclusion that the simple binary classification of MAO into MOA-A and MAO-B is an oversimplification. 43 references. (Author abstract modified)

002913 Frankel, David; Khanna, Jatinder M.; Kalant, Harold; LeBlanc, A. Eugene. Department of Pharmacology, University of Toronto, Toronto, Canada M5S 1A8 **Effect of p-chlorophenylalanine on the acquisition of tolerance to the hypothermic effects of alcohol.** Psychopharmacology (Berlin). 57(3):239-242, 1978.

Daily administration of ethanol in a liquid diet or by intubation produced tolerance to the hypothermic effects of ethanol in male Sprague-Dawley rats. When p-chlorophenylalanine (PCPA) was administered in a dose previously shown to maintain extensive depletion of brain serotonin (5-HT), the temperature lowering effects of ethanol were less pronounced than in controls. The analysis of the effect of PCPA on tolerance development took into account both initial body temperature and the degree of hypothermia. Results suggest that 5-HT may have a role in the development of tolerance to ethanol. 12 references. (Author abstract modified)

002914 Freed, Curt R.; Quintero, Emperatriz; Murphy, Robert C. Department of Medicine, Division of Clinical Pharmacology, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver, CO 80262 **Hypotension and hypothalamic amine metabolism after long-term alpha-methyldopa infusions.** Life Sciences. 23(4):313-322, 1978.

To identify the metabolite of alpha-methyldopa (aMD) most responsible for the hypotensive effect of the drug, aMD was infused (2-20mg/kg/hour) into the jugular vein of normotensive, conscious, restrained male Sprague-Dawley rats. Changes in blood pressure were measured after 24 hours of drug infusion. Steady state turnover was then determined by switching infusions to identical doses of deuterated aMD (2,5,6-aMD-d3) and the rate of incorporation of deuterium into the metabolites alpha-methyldopamine (aMDA) and alpha-methylnorepinephrine (aMNE) was followed. Results show that blood pressure reduction was correlated with aMDA concentration but not with aMNE concentration or turnover rate. 19 references. (Author abstract)

002915 Frenk, Hanan; McCarty, Bradford C.; Liebeskind, John C. Department of Psychology, Tel-Aviv University, Ramat Aviv, Israel **Different brain areas mediate the analgesic and epileptic properties of enkephalin.** Science. 200(4339):335-337, 1978.

Single injections of 120mg of methionine enkephalin were made into various midbrain and forebrain structures in the rat. Analgesia was observed after injections into or near the ventral, caudal midbrain periaqueductal gray matter. Seizures and other pathological electroencephalogram (EEG) changes were observed with injections into or near the forebrain dorsomedial nucleus of the thalamus. No animals with midbrain injection sites showed EEG changes, and none with forebrain injection sites were analgesic. The data, taken together with other lines of evidence, suggest that enkephalin-induced analgesia and enkephalin-induced seizures are mediate by opiate receptors that are located in different brain areas and that are pharmacologically different. 22 references. (Author abstract)

002916 Frenk, Hanan; Urca, Gideon; Liebeskind, John C. Department of Psychology, Tel Aviv University, Ramat Aviv, Israel **Epileptic properties of leucine- and methionine-enkephalin: comparison with morphine and reversibility by naloxone.** Brain Research (Amsterdam). 147(2):327-337, 1978.

Morphologically similar epileptic seizures were recorded from the cortex of rats after injections into the lateral ventricle of 100 micrograms of leucine-enkephalin, methionine-enkephalin, and morphine. Seizures were either greatly attenuated or blocked completely by prior systemic administration of naloxone (10mg/kg), indicating that the seizures resulted from the interaction of the compounds with opiate receptors in the brain. Seizures and other pathological manifestations could be elicited by enkephalin doses as low as 10 micrograms. Leucine-enkephalin had greater epileptic potency than methionine-enkephalin. At doses of 1 microgram, both enkephalins typically evoked cortical spindles resembling those seen in drowsy animals. Enkephalin-induced analgesia was seen in only one animal at the 100 microgram dose. The endogenous enkephalins appear to play a role in normal mechanisms of reward, as well as contributing to the elaboration of certain epileptic phenomena. 32 references. (Author abstract modified)

002917 Friedle, N. M.; Kelly, P. H.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Regional brain atrophy and reductions in glutamate release and uptake after intrastriatal kainic acid.** British Journal of Pharmacology (London). 63(1):151-158, 1978.

Neurochemical changes and tissue weights were measured following intrastriatal injection of kainic acid (2.5mcg in 2mcl of 0.9% saline) in adult male Sprague-Dawley rats. After kainic acid, the striatum and neocortex on the injected side showed a progressive reduction in weight, the neocortex showing the greatest absolute weight loss and the striatum the greatest percentage change. Large (80-90%) reductions in choline acetyl-

transferase (CAT) and L-glutamate decarboxylase (GAD) activities in the striatum occurred within 2-4 days of the injection and persisted at least 10 weeks. At 10 weeks, CAT and GAD activities were unaltered in the neocortex. The absolute content of dopamine in the striatum was not different from control 5 days after the injection of kainic acid but reduced at 2 and 10 weeks; at 2 weeks the concentration of dopamine (mcg/g wet weight) of dopamine was also reduced, but at 10 weeks it was near normal, due to atrophy of the striatum. The high affinity glutamate uptake into a crude synaptosomal preparation of the striatum was reduced by 64% 5 days after kainic acid and by 67% at 10 weeks. In vitro kainic acid neither altered the high affinity uptake of radiolabelled glutamate into a homogenate of the striatum nor released endogenous glutamate from slices of striatum. 25 references. (Author abstract modified)

002918 Fuller, Ray W.; Hemrick, Susan K. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 64206 **Steric influence on inhibition of monoamine oxidase forms by 2,3-dichloro-alpha-methylbenzylamine.** Research Communications in Chemical Pathology and Pharmacology. 20(1):199-202, 1978.

Steric influence on inhibition of monoamine oxidase (MAO) forms by 2,3-dichloro-alpha-methylbenzylamine in rat brain is reported. The () isomer of 2,3-dichloro-alpha-methylbenzylamine inhibited the oxidation of serotonin, a substrate of type-A MAO, by rat brain mitochondrial MAO more effectively than it inhibited the oxidation of phenylethylamine, a substrate for type-B MAO. In contrast, the (-) isomer inhibited phenylethylamine oxidation more than it inhibited serotonin oxidation. These were found to be the first pair of stereoisomers observed to have opposite selectivity as inhibitors of type-A and type-B MAO. 2 references. (Author abstract modified)

002919 Fuller, Ray W.; Perry, Kenneth W.; Bymaster, Frank P.; Wong, David T. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Comparative effects of pemoline, amfonelic acid and amphetamine on dopamine uptake and release in vitro and on brain 3,4-dihydroxyphenylacetic acid concentration in spiperone-treated rats.** Journal of Pharmacy and Pharmacology (London). 30(3):197-198, 1978.

The comparative effects of pemoline, amphetamine, and amfonelic acid on (3H)dopamine accumulation in rat striatal synaptosomes and on the spiperone-induced elevation of 3,4-dihydroxyphenylacetic acid (DOPAC) in rat brain were examined in vitro and in vivo. Amfonelic acid and amphetamine similarly inhibited dopamine uptake into synaptosomes in vitro but caused opposite changes in brain dopamine in vivo. Results indicate that pemoline does not affect brain dopamine neurons in the same way as amfonelic acid, rather its action may be qualitatively like that of amphetamine. In vitro pemoline is a weaker inhibitor of dopamine uptake than amphetamine, and in vivo it lowers brain DOPAC concentration to a lesser extent than does amphetamine. 10 references.

002920 Gainer, Harold, Brownstein, Michael J. Behavioral Biology Branch, National Institute for Child Health and Human Development, Bethesda, MD 20014 **Electrophoretic analyses of proteins transported to the rat posterior pituitary.** Journal of Neurochemistry (Oxford). 30(6):1509-1512, 1978.

The labelling patterns of proteins transported from the hypothalamus to the posterior pituitary using three different labelled precursors, (355)cysteine, (3H)methionine, and (3H)fucose were compared. The three precursors were injected into the supraoptic nuclei (SON) of rats, and the labelled proteins that were transported to and accumulated in the posterior pituitary 24 hr postinjection were analyzed electrophoretically. The transported, labelled proteins which were soluble in 0.1M HCl were primarily of low molecular weight. However, the selectivity of labelling of these proteins by the three different labelled precursors could be revealed by isoelectric focusing. The 0.1M HCl insoluble labelled proteins, presumably reflecting membrane proteins transported from the SON to the pituitary, were more diverse and generally of higher molecular weight. 20 references. (Author abstract)

002921 Gartside, I. B. Department of Pharmacology, School of Pharmacy, Brunswick Square, London WC1N 1AX, England **The actions of diazepam and phenytoin on a low dose penicillin epileptiform focus in the anaesthetised rat.** British Journal of Pharmacology (London). 62(2):289-292, 1978.

A technique is described for the induction of an acute short-lived epileptiform focus by the local injection of benzyl penicillin (25 units) into the cerebral cortex of rats anesthetized with urethane. The effects of anticonvulsants on this microfocus were studied. Phenytoin (20mg/kg) and diazepam (1mg/kg), given intravenously, significantly reduced the frequency of the normally occurring surface positive electrocorticogram plateaux and caused a greater decrease in the frequency of the epileptiform spikes normally associated with these plateaux. A novel effect was seen in that both anticonvulsant drugs significantly reduced the amplitude of the epileptiform spike within the focus, as well as causing an even larger decrease in the amplitude of the propagated spike. The contribution of the anticonvulsant drug effect on the focal spike to its effect on propagated activity is discussed. 4 references. (Author abstract)

002922 Geisler, A.; Klysner, R. Department of Pharmacology, University of Copenhagen, Juliane Maries Vej 20, Copenhagen, Denmark **Influence of lithium on dopamine-stimulated adenylate cyclase activity in rat brain.** Life Sciences (Oxford). 23(6):635-636, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical approaches, held in Beerse, Belgium, July 1978, the effect of lithium on dopamine stimulated adenylate cyclase activity in male Wistar rat brain is reported. Lithium inhibited dopamine stimulated adenylate cyclase activity in vitro in a dose dependent and noncompetitive fashion. No changes in enzyme activity were observed in lithium treated rats. 9 references. (Author abstract modified)

002923 Gilbert, J. C.; Allen, J. M.; Townsend, B. G.; Wyllie, M. G. Pharmacology Section, Department of Pharmacy, Heriot-Watt University, Edinburgh, EH1 2HJ, Scotland **Drugs affecting the central nervous system: effects of pemoline, and tricyclic antidepressants on nerve terminal adenosine triphosphatase activities and neurotransmitter release.** Neuropharmacology (Oxford). 17(6):419-421, 1978.

The effects of pemoline, protriptyline, nortriptyline, amitriptyline, and ouabain on the adensoine triphosphatases (ATPases) which catalyze the hydrolysis of ATP in the presence of several different cations were examined in the rat synaptosome. Tricyclic antidepressants inhibited all of the ATPases tested (Na, Mg2, Ca2, and Na, K), while ouabain and pemoline only affected the Na, KATPase. The effect of pemoline on this enzyme was clearly biphasic; at high concentrations, pemoline inhibited the enzyme, whereas at low concentrations the effect was one of stimulation. These effects of pemoline were reflected by the effects of the drug on norepinephrine release. Findings suggest an inverse relationship between the activity of nerve terminal Na, KATPase and norepinephrine release. 5 references.

002924 Gilbert, J. C.; Davison, D. V.; Wyllie, M. G. Pharmacology Section, Department of Pharmacy, Heriot-Watt University, Edinburgh, EH1 2HJ, Scotland **Studies of the physiological**

roles of prostaglandins in the central nervous system. Neuropharmacology (Oxford). 17(6):417-419, 1978.

The effects of depolarizing conditions such as electrical stimulation, potassium ion addition, and veratridine addition on the release of prostaglandins and noradrenaline (NE) from rat synaptosomes were determined. The effect of depolarization on acetylcholine (ACh) release and the effects of exogenous prostaglandins on the subsequent release of NE from synaptosomes under basal and evoked conditions were also explored. In the rat synaptosome preparation, prostaglandin release was spontaneous and was not significantly altered by any of the conditions used to depolarize the synaptosomes. Both high potassium ion concentration and electrical stimulation significantly increased ACh release; NE release was significantly increased by these conditions as well as by the addition of veratridine. The addition of exogenous prostaglandins had no effect on NE release from synaptosomes under basal or potassium depolarized conditions. Results suggest that it is unlikely that prostaglandins act as neurotransmitters or neuromodulators of NE in the central nervous system. 9 references.

002925 Glatt, A.; Klebs, K.; Koella, W. P. Biological Research Laboratories, Pharmaceuticals Division, CIBA-GEIGY Ltd., Basel, Switzerland **Influence of vincamine and piracetam on sleep-waking pattern of the cat.** Biological Psychiatry. 13(4):417-427, 1978.

The effect of Vincamine and Piracetam, two geriatric drugs, on sleep behavior of the laboratory cat was studied. The animals were chronically prepared for recording of the EEG of the cerebral cortex, the lateral geniculate body, and the hippocampus, and for recording of eye movements, the muscular tonus and respiration. During the experiment, sleep and walking behavior were monitored by the above mentioned telemetrically transmitted indicators and also through observation via closed circuit television. Both Vincamine and Piracetam in doses of 1 and 300mg/kg p.o.,respectively, enhance absolute and relative amounts of paradoxical sleep (PS). Smaller doses have a lesser or no effect on PS. Larger doses again have little effect or else, in the first few hours after application, reduce PS and total amount of sleep. Both drugs have little effect on slow wave and total sleep. Piracetam, but not Vincamine, reduces the prominent frequency of the theta band in hippocampus during PS. The PS enhancing effect of the two geriatric drugs may be related to their memory improving influence. 31 references. (Author abstract)

002926 Gold, Mark S.; Redmond, D. Eugene, Jr.; Donabedian, Richard K.; Goodwin, Frederick K.; Extein, Irl. Fair Oaks Hospital, 19 Prospect St.; Summit, NJ 07901 **Increase in serum prolactin by exogenous and endogenous opiates: evidence for antidopamine and antipsychotic effects.** American Journal of Psychiatry. 135(11):1415-1416, 1978.

The increase in serum prolactin by exogenous and endogenous opiates was investigated to evaluate a prolactin stimulation model for screening new antipsychotic compounds. The effects of morphine and of FK 33-824, a synthetic d-alanine methionine-enkephalin derivative, on serum prolactin in macaque monkeys, were studied following a month of acclimatization to the sample collection procedure. Data support speculations, behavioral studies, anecdotal reports from the era before antipsychotic medication, clinical experience in methadone maintenance programs, and recent pilot studies with psychotic humans that opiate agonists may be antipsychotic in man. 10 references.

002927 Goldberg, Leon I.; Volkman, Paul H.; Kohli, Jai D. Department of Pharmacological and Physiological Sciences, University of Chicago, Chicago, IL 60637 **A comparison of the vascular dopamine receptor with other dopamine receptors.** Annual Review of Pharmacology and Toxicology. 18:57-79, 1978.

Similarities and differences in the effects of agonists and antagonists acting on the dopamine (DA) receptor in the canine renal vascular bed and on selected DA receptors in other organs and species are reviewed. Characterization of receptors by classical physiological techniques requires demonstration of certain conditions which have not been met in studies of the DA receptor, primarily because they require a suitable isolated organ system. Through use of renal artery vasodilation following intraarterial injections of DA and a series of agonists, the following criteria have been fulfilled: 1) opposing vasoconstricting actions of DA and most DA agonists can be blocked by phenoxybenzamine; 2) specific antagonism can be demonstrated with a dose of antagonist that does not affect other vasodilators; 3) beta-adrengeric, cholinergic, histaminergic, serotonergic, and neurogenic influences can be eliminated; and 4) the same order of potency of agonists and antagonists has been demonstrated in both the renal and mesenteric vascular beds. If structural requirements for action on the vascular DA receptor are accepted as valid, an explanation must be found for the marked qualitative and quantitative discrepancies found when comparing results obtained with the canine renal artery to other organs and tissues. 145 references. (Author abstract modified)

002928 Gordon, J. L.; Olverman, H. J. ARC Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **5-Hydroxytryptamine and dopamine transport by rat and human blood platelets.** British Journal of Pharmacology (London). 62(2):219-226, 1978.

The uptake of 5-hydroxytryptamine (5-HT) and dopamine (DA) by rat platelets were compared with respect to the kinetics and pharmacology of the processes, to determine whether platelets may be suitable models for studying uptake mechanisms in dopaminergic and serotoninergic neurons. Uptake of 5-HT by rat platelets in plasma was very rapid and diffusion did not contribute significantly at substrate concentrations that did not saturate the active transport. Kinetic analysis revealed a high affinity uptake mechanism for 5-HT. DA uptake was relatively slow and involved a lower affinity active transport process. Diffusion contributed significantly at concentrations that did not saturate the active transport. Serotonin competitively inhibited uptake of DA and vice versa. Chlorimipramine, desmethylimipramine and benztropine were tested as uptake inhibitors. Each was equipotent against 5-HT and DA, although the absolute potency of the drugs varied greatly. Chlorimipramine was the most potent and kinetic analysis revealed that this inhibition was competitive against both 5-HT and DA. Similar results were obtained in studies with human platelets. DA is actively transported by platelets via the 5-HT uptake mechanism, but with a much lower affinity. There is no high affinity DA specific mechanism corresponding to that in the corpus striatum. Although platelets may be valid models of transport in 5-HT neurons, they should not be regarded as models for the DA transport mechanism found in dopaminergic neurons. 29 references. (Author abstract modified)

002929 Gorissen, H.; Laduron, P. M. Department of Biochemical Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Solubilization of 3H-spiperone binding sites from rat brain.** Life Sciences (Oxford). 23(6):575-579, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the use of digitonin to solubilize 3H-spiperone binding sites from Wistar rat striatum and frontal

cortex is reported. The ligand/macromolecular complex was separated from the free ligand by gel filtration. Neuroleptic drugs had a lower affinity for the soluble preparation than for the membrane bound receptors; however, the soluble preparation displayed stereospecific properties. Although the nature of this solubilized component is still unknown, results of a thermal inactivation experiment suggest that it is a macromolecular complex extracted from membranes bearing neuroleptic receptors in the striatum and frontal cortex. 14 references. (Author abstract modified)

002930 Gourlay, Geoffrey K.; Stock, Beresford H. School of Pharmacy, South Australian Institute of Technology, North Terrace, Adelaide, SA 5000, Australia **Pyridine nucleotide involvement in rat hepatic microsomal drug metabolism -- III. The influence of the 1,4,5,6-tetrahydronicotinamide analogue of NADH on the NADPH kinetics of aminopyrine-N-demethylation.** Biochemical Pharmacology (Oxford). 27(6):979-983, 1978.

In a study of Wistar rat hepatic microsomal drug metabolism, a structural analogue of the reduced form of nicotinamide dinucleotide (NADH), 1,4,5,6-tetrahydronicotinamide adenine dinucleotide (NADH3), was unable to support the demethylation of aminopyrine or the reduction of the cytochrome P450/aminopyrine complex. The combination of NADH3 with the reduced form of nicotinamide dinucleotide phosphate (NADPH) stimulated the NADPH dependent reduction of the cytochrome P450/aminopyrine complex. When the kinetic constants were determined in the presence of 100mcM NADH3, there was no significant alteration in the apparent Michaelis-Menten constant (Km) (NADPH) value, but there was an 80% increase in apparent velocity of NADPH for NADPH/cytochrome P450 reductase. The inclusion of NADH3 in the medium for aminopyrine demethylation resulted in a significant increase in apparent velocity compared to the value obtained in the absence of NADH3. Results suggest that the structure of NADH, as well as its capacity to donate the electron, is responsible for the NADH mediated increase in aminopyrine metabolism. 14 references. (Author abstract modified)

002931 Gourlay, Geoffrey K.; Stock, Beresford H. School of Pharmacy, South Australian Institute of Technology, North Terrace, Adelaide, SA 5000, Australia **Pyridine nucleotide involvement in rat hepatic microsomal drug metabolism -- I. Factors that influence NADPH kinetic estimations during mixed function oxidase reactions.** Biochemical Pharmacology (Oxford). 27(6):965-968, 1978.

The hypothesis that the localization of significant amounts of nucleotide pyrophosphatase activity in the Wistar rat hepatic microsomal fraction would result in erroneous values of the apparent Michaelis-Menten constant (Km) (nicotinamide adenine dinucleotide phosphate reduced form, NADPH) for aminopyreine-N-demethylase was tested. The inclusion of 20mM pyrophosphate into the rat liver inhibited nucleotide pyrophosphatase activity and reduced the apparent Km (NADPH) value from 27.9mcM to 7.92 mcM. The apparent Km (NADPH) values determined in the presence of three type 1 substrates were not statistically different from each other, but the value in the presence of aniline was lower. The kinetic constants of NADPH for NADPH/cytochrome P450 reductase in the presence of either aminopyrine, ethylmorphine or aniline, were also determined. 40 references. (Author abstract modified)

002932 Gourlay, Geoffrey K.; Stock, Beresford H. School of Pharmacy, South Australian Institute of Technology, North Terrace, Adelaide, SA 5000, Australia **Pyridine nucleotide involvement in rat hepatic microsomal drug metabolism -- II. Evidence for a co-operative interaction between NADPH and NADH.** Biochemical Pharmacology (Oxford). 27(6):969-978, 1978.

In a study of Wistar rat hepatic microsomal drug metabolism, a significant reduction in apparent Michaelis-Menten (Km) nicotinamide adenine dinucleotide phosphate reduced form, NADPH) values for both aminopyrine and ethylmorphine demethylases was observed when the kinetic constants for NADPH were determined in the presence of constsnt nicotinamide adenine dinucleotide reduced (NADH) concentrations. NADH significantly stimulated apparent velocity values for NADPH/cytochrome P450 reductase in the presence of aminopyrine, without changing the apparent km (NADPH) value. NADPH stimulated the initial rapid phase of the biphasic reduction kinetics of NADPH/cytochrome P450 reductase in the presence of aminopyrine. Findings suggest that in the presence of both pyridine nucleotides, there was a change in the rate limiting step which, with NADPH alone, is generally accepted to be the reduction of the cytochrome P450 substrate complex. 52 references. (Author abstract modified)

002933 Greenberg, R. Squibb Institute for Medical Research, P. O. Box 4000, Princeton, NJ 08540 **The neuronal origin of prostaglandin released from the rabbit portal vein in response to electrical stimulation.** British Journal of Pharmacology (London). 63(1):79-85, 1978.

Transmural electrical stimulation of the isolated portal vein of the male albino rabbit was accompanied by the release of a prostaglandin-like substance (PLS). Thin layer chromatography coupled with bioassay indicates that this substance was probably prostaglandin E2. Indomethacin potentiated the response of the portal vein to electrical stimulation at 2 Hz and abolished the release of the PLS. There was no significant change in the amount of PLS released from the portal vein in response to electrical stimulation at 2 Hz when the contractile response of the portal vein was prevented by pretreatment with phentolamine or guanethidine. In vitro denervation of the portal vein with 6-hydroxydopamine or the omission of calcium from the bathing solution caused a significant reduction in the amount of PLS released from the portal vein in response to electrical stimulation at 2 Hz. It is concluded that electrical stimulation of the isolated portal vein of the rabbit is accompanied by the release of a PLS from a neuronal source. 21 references. (Author abstract modified)

002934 Griffin, W. S. T.; Woodward, D. J.; Chanda, R. University of Texas, Health Science Center, Dallas, TX 75235 **DNA synthetic ability in cerebella from temperature and handling stressed neonatal rats.** Brain Research Bulletin. 3(4):365-367, 1978.

DNA synthetic ability of neonatal Wistar rat cerebellum was studied in two stressful conditions (cooling and excessive handling) which may be inadvertently imposed during the course of certain experiments. A rate study of the ability of animals handled excessively for 10 minutes to incorporate 14C-thymidine into the DNA tissue fraction (DNAF) from the acid soluble tissue fraction (ASF) of the cerebellum revealed a decreased DNA synthetic ability which lasted for 1 hour. Animals with very low core temperatures incorporated little 14C into the DNAF from the ASF 2 hours after an IP injection of 14C-thymidine. There was a proportional decrease in the ability to synthesize DNA as core temperature decreased. The results demonstrate the importance of controlling for various stresses that may be concomitantly applied in experimental paradigms. 7 references. (Author abstract)

002935 Gronan, Robert J.; York, Donald H. Department of Physiology, School of Medicine, University of Missouri, Colum-

bia, MO 65212 **Effects of angiotensin II and acetylcholine on neurons in the preoptic area.** Brain Research (Amsterdam). 154(1):172-177, 1978.

The effects of microiontophoretically applied angiotensin II and acetylcholine (ACh) on neurons in the preoptic area of male Sprague-Dawley rats were studied. Angiotensin II excited a high proportion of neurons in the medial preoptic area, many of which were also excited by ACh. The increased frequency of cell discharge with angiotensin II application suggests a direct mechanism of action on neuronal elements of this region. The presence of sensitive units in this area is consistent with evidence identifying the anterior third ventricle region as an important site for the dipsogenic and pressor actions of angiotensin II. 22 references.

002936 Guellaen, Georges; Mahu, Jean-Louis; Mavier, Philippe; Hanoune, Jacques; Berthelot, Pierre. Unite de Recherches INSERM U-99, Hopital Henri Mondor, 94010 Creteil, France **Non-specific inhibition of some rat liver membrane-bound enzymes by an adenylate cyclase inhibitor, RMI 12330 A.** Biochemical Pharmacology (Oxford). 27(5):641-645, 1978.

The effects of RMI-12330A (N-(cis-2-phenylcyclopentyl) azacyclotridecan-2-imine hydrochloride) on adenylate cyclase activity in particulate fractions of brain, spleen, heart, kidney and in liver plasma membrane preparations were examined in female Wistar rats. In plasma membrane preparations, this agent inhibited the activities of magnesium ion adenosine triphosphatase and leucyl-beta-naphthylamidase but had no effect on 5'nucleotidase. In nonactivated liver microsomes, the activities of p-nitrophenol and bilirubin uridine diphosphate-glucuronosyltransferases and of glucose-6-phosphatase were enhanced by low concentrations of RMI-12330A but inhibited by higher concentrations. This biphasic effect disappeared when digitonin activated or Emulgen 911 solubilized microsomal membranes were used. It is concluded that RMI-12330A does not behave as a specific inhibitor of adenylate cyclase, since it also perturbs other membrane associated enzyme activities. 34 references. (Author abstract modified)

002937 Halaris, Angelos E.; DeMet, Edward M. University of Chicago, Department of Psychiatry, 950 East 59th Street, Chicago, IL 60637 **Active uptake of (3H)5-HT by synaptic vesicles from rat brain.** Journal of Neurochemistry (Oxford). 31(3):591-597, 1978.

The uptake of tritiated 5-hydroxytryptamine (3H-5HT) was studied in synaptosomal suspensions and vesicular fractions from male Sprague-Dawley rat brain. Arrhenius plots for synaptosomes differed from those for vesicles, as did the temperature coefficients for these two fractions. In the presence of adenosine triphosphate (ATP), vesicular uptake was stimulated approximately eightfold. Ouabain, dinitrophenol, and N-ethylmaleimide (NEM) inhibited synaptosomal uptake but failed to affect 3H-5HT accumulation by vesicles in the absence of ATP. When ATP was added, vesicular uptake was also blocked by NEM but was unaffected by ouabain or 2,4-dinitrophenol. Total uptake consisted of two components, one ATP dependent and the other nonsaturable and ATP independent. Active vesicular 3H-5HT uptake was magnesium dependent and was inhibited by sodium and potassium. Cation effects on uptake were specific and could not be accounted for by changes in osmotic pressure or ionic strength. It is concluded that synaptic vesicles from whole rat brain accumulate 3H-5HT by an active process. 17 references. (Author abstract modified)

002938 Harms, Herman H.; Wardeh, George; Mulder, Arie H. Department of Pharmacology, Free University, Van der Boechorstraat 7, Amsterdam, The Netherlands **Adenosine modulates depolarization-induced release of 3H-noradrenaline from slices of rat brain neocortex.** European Journal of Pharmacology (Amsterdam). 49(3):305-308, 1978.

The effects of adenosine and some related purines on the potassium-induced release of tritiated noradrenaline (3H-NA) from male Wistar rat cerebral cortex slices were determined in a superfusion system. Adenosine and adenosine triphosphate caused a dose dependent inhibition of 3H-NA release, with a maximal effect of 35% at 0.0001M. Theophylline, 0.0001M, antagonized the inhibitory effect of adenosine. Results support the hypothesis that at least some of the central stimulant effects of the methylxanthines is related to blockade of a purinergic inhibitory tone on noradrenergic synaptic output. 10 references. (Author abstract)

002939 Harris, Ward E.; Stahl, William L. Neurochemistry Laboratory, Veterans Administration Hospital, GMR-151, 4435 Beacon Avenue South, Seattle, WA 98108 **Interactions of adrenergic compounds with brain membrane constituents.** Biochemical Pharmacology (Oxford). 27(16):2015-2019, 1978.

The specific activity of sodium ion/postassium ion stimulated adenosine triphosphatase of synaptosomes from male Sprague-Dawley rat brains was modulated by a series of adrenergic compounds in a manner related to each compound's partition between aqueous and organic solvents. The more organic soluble compounds (the beta-2-adrenergic blockers propranolol, pronethalol, and butoxamine) inhibited the enzyme by 13-30%. The more a queous soluble compounds (the agonists epinephrine, norepinephrine, and isoproterenol, and the beta-1-adrenergic blockers, practolol and acebutolol) stimulated the enzymatic activity by 30%. These effects may be due to nonspecific membrane interactions rather than to specific receptor effects. Optical measurements with pure protein and phospholipid indicate that the aqueous soluble compounds bound to protein, while the organic soluble compounds interacted with acidic phospholipid phosphatidly serine. The possible consequences of the compounds binding with acidic phospholipids and the resulting effect of membrane properties are discussed. 18 references. (Author abstract)

002940 Hauser, Danie; Closse, Annemarie. Sandoz Ltd., Pharmaceutical Division, Chemical Research, CH-4002 Basle, Switzerland **3H-clozapine binding to rat brain membranes.** Life Sciences (Oxford). 23(6):557-561, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, characteristics of tritiated clozapine binding to rat brain membranes are described. Binding studies indicated that 3H-clozapine binds specifically and with high affinity (dissociation constant, 1.3nM) to rat brain membranes. About two thirds of reversibly bound 3H-clozapine was displaced by hyoscyamine in a stereospecific manner, suggesting interaction of clozapine with muscarinic cholinergic receptors. Most of the remaining 3H-clozapine binding was stereospecifically inhibited by butaclamol, but this binding component did not appear to be related to dopamine receptors. 15 references. (Author abstract modified)

002941 Hawkins, Morris, Jr.; Breakefield, Xandra O. Dept. of Human Genetics, Yale University School of Medicine, New Haven, CT 06510 **Monoamine oxidase A and B in clultured cells.** Journal of Neurochemistry (Oxford). 30(6):1391-1397, 1978.

Monoamine oxidase (MAO) activity against tryptamine was compared in a number of continuous rodent lines, including neuroblastoma, hepatoma, melanoma, nephroma, sarcoma, and L cells. Activities against tryptamine varied over 300 fold in homogenates of different lines, being highest in hepatoma line MH1C1 and lowest in a neuroblastoma line lacking hypoxanth-

ine phosphoribosyltransferase (HPRT) activity. The amount, but not the type, of MAO activity varied with the stage of growth in homogenates of neuroblastoma and hepatoma cells. Measurements of sucinate-cytochrome c reductase (SccR), another mitochondrial enzyme, also showed 20 fold variations between lines, being highest in neuroblastoma line N1E-115 and lowest in hepatoma line MH1C1; SCCR and MAO activities appeared to be regulated independently. The relative proportions of the A and B types of MAO activity were determined in homogenates and living cultures. Clorgyline inhibition of tryptamine deamination homogenates indicated that in all lines except MH1C1, greater than 95% of the MAO activity was of the A type. In MH11 homogenates, using clorgyline or deprenyl, 40-70% of the activity appeared to be of the A type and 30-60% of the B type. In cultures of neuroblastoma N1E-115 cells, deamination of tryptamine and dopamine was sensitive to inhibition by low concentrations of clorgyline, indicating that the A type of activity is present intracellularly, as in homogenates. In MHICI hepatoma cultures, tryptamine deamination showed a biphasic senisitivity to clorgyline. This interpreted to mean that A and B types of MAO activity occur together in living hepatoma cells. 27 references. (Author abstract)

002942 Heal, D. J.; Green, A. R.; Bloomfield, M. R.; Grahame-Smith, D. G. MRC Unit and University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford, OX2 6HE, U.K. **Neuroleptic drugs block both the hyperactivity and the increase in caudate nucleus cyclic AMP concentration produced by the administration of tranylcypromine and L-dopa to rats.** Psychopharmacology (Berlin). 57(2):193-197, 1978.

Injection of adult male Sprague-Dawley rats with tranylcypromine and L-dopa increased brain dopamine concentrations and produced a behavioral syndrome that included hyperactivity. It also elevated caudate nucleus cyclic adenosine monophosphate (AMP) concentrations by about 50% in vivo, probably by stimulating dopamine receptors. Pretreatment with chlorpromazine inhibited both the tranylcypromine/L-dopa-induced behavior and elevated cyclic AMP concentrations in a dose dependent manner. Haloperidol and alpha-flupenthixol also inhibited both effects, while beta-flupenthixol and pimozide were without effect. Since none of these drugs altered the tranylcypromine/L-dopa-induced rise of brain dopamine, it is likely that they produced their effect by inhibiting dopamine sensitive adenylate cyclase. A correlation was found to exist between the neuroleptic inhibition of both the increased behavioral activity and the increased caudate nucleus cyclic AMP concentrations produced by tranylcypromine and L-dopa. 23 references. (Author abstract)

002943 Henn, F. A.; Henke, D. J. Neurochemical Research Laboratories, Dept. of Psychiatry, College of Medicine, University of Iowa, 500 Newton Road, Iowa City, IA 52242 **Cellular localization of (3H)-diazepam receptors.** Neuropharmacology (Oxford). 17(11):985-988, 1978.

Isolated fractions enriched in bovine cortical astroglial cells or nerve endings were used to determine the receptor site for (3H)-diazepam binding. The results suggest strong enrichment in glial cells for the benzodiazepine receptor. Both the inhibition of diazepam binding by other benzodiazepines and the affinity of the glial receptor for diazepam suggest that this receptor is similar to that previously reported in crude CNS membrane fractions. 10 references. (Author abstract)

002944 Henn, F. A.; Titeler, M.; Aderson, D. J.; May, K. Neurochemistry Research Laboratories, Department of Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242 **Investigations concerning the cellular origin of dopamine receptors.** Life Sciences (Oxford). 23(6):617-622, 1978.

In a paper presented at teh Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium July 1978, studies of dopamine receptors in glial cell fractions and synaptic fractions prepared from bovine brain are described. No evidence of haloperidol binding was found in neuronal, glial, or synaptosomal fractions from bovine substantia nigra. However, binding studies using apomorphine, spiroperidol and haloperidol in bovine caudate atroglia and synaptosomes support the astroglial localization of a significant portion of dopamine receptors. Autoradiographic studies of rat caudate also suggest that a significant portion of the dopamine receptors in rat striatum are associated with astroglial cells. 8 references. (Author abstract modified)

002945 Herink, J.; Fusek, J.; Bajgar, J.; Patocka, J.; Hrdina, V. Purkyne Medical Research Institute, 50260 Hradec Kralove, Czechoslovakia **Interaction of imipramine and 3-quinuclidyl benzilate with 9-amino-7-methoxy-1,2,3,4-tetrahydroacridine on the after-discharges in the limbic system.** Activitas Nervosa Superior (Praha). 20(1):79-80, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the interaction of imipramine and 3-quinuclidyl benzilate (QB) with 9-amino-7-methoxy-1,2,3,4-tetrahydroacridine (TA03) on the after discharges in the limbic system is described. Imipramine had a facilitative effect on the duration of after discharges in the limbic system of male albino Wistar rats, while amplitude was not influenced. TA03 delayed the onset of imipraimine effect, and the amplitude of after discharges was increased. QB decreased both parameters for 20 to 30 min. This suppression was followed by an increase in the duration and amplitude. TA03 blocked the initial impairment and delayed the onset of the consecutive facilitation without its suppression. 3 references.

002946 Hertz, Leif; Mukerji, Srimathie; Boechler, Norma. Department of Anatomy, University of Saskatchewan, Saskatoon, Saskatchewan, S7N OWO, Canada **Phenobarbital effect on glial cell respiration in the presence of a high concentration of potassium.** Biochemical Pharmacology (Oxford). 27(6):903-905, 1978.

Rates of oxygen uptake were measured micromanometrically in samples of 55 morphologically differentiated astrocytes obtained from primary cultures grown from the dissociated cerebral hemispheres of newborn DBA mice. With a low potassium concentration (5mM) in the medium, the respiration was high and well maintained. Exposure to an increased potassium concentration (55mM) led to a rapid decline in the rate of oxygen uptake. It was found that this decline was prevented by 0.5-1.OmM phenobarbital, which had no effect on respiration in the medium containing 5mM potassium. 28 references. (Author abstract)

002947 Hesketh, John; Glen, Iain. MRC Brain Metabolism Unit, University Department of Pharmacology, 1 George Square, Edinburgh, Scotland **Lithium transport from cerebrospinal fluid.** Biochemical Pharmacology (Oxford). 27(5):813-814, 1978.

In male New Zealand white rabbits, lithium was lost from the cerebrospinal fluid (CSF) containing spaces during perfusion of the ventricles with artificial CSF containing 1mM lithium chloride. This loss of lithium was characterized by a transport constant that suggested that lithium left the CSF by passive diffusion. The small amount (16%) of lithium recovered in the brain showed that little lithium penetrated the intracellular space of the brain. The lack of active removal of lithium by the choroid plexus under experimental conditions, similar to those in which lithium stimulates choroid plexus sodium transport, suggests that

active lithium transport is not necessary for lithium to stimulate the sodium pump. 15 references. (Author abstract)

002948 Hewick, D. S.; Shaw, V.; Department of Pharmacology and Therapeutics, University of Dundee Medical School, Ninewells Hospital, Dundee, DD1 9SY, Scotland **Tissue distribution of radioactivity after injection of (14C) nitrazepam in young and old rats.** Journal of Pharamacy and Pharmacology (London). 30(5):318-319, 1978.

A study to determine tissue distribution of nitrazepam in Wistar rats was conducted with special emphasis on the problem of age related nitrazepam sensitivity. Young rats (100 days old) and old rats (540 days old) were injected with nitrazepam intraperitoneally to avoid any age related variation in drug absorption from the gastrointestinal tract. Nitrazepam plasma half lives were calculated from a least squares regression analysis of logarithm of plasma nitrazepam concentration vs. time plots. Old rats were visibly more sedated by the dose, but plasma concentrations of radioacitvity were similar in both animals. Highest concentrations of radioactivity were found in the kidney and the liver, followed by spleen, heart and lung, with the lowest concentration in the plasma and brain. It is suggested that any analogous distribution change in man could account, wholly or in part, for the increased sensitivity to nitrazepam seen in elderly people. 6 references.

002949 Ho, W. K. K.; Lam, S.; Leung, K. C.; Au, K. K.; Wong, H. K.; Tsang, Y. F.; Wen, H. L. Department of Biochemistry, Chinese University of Hong Kong, Shatin, Hong Kong **Effect of naloxone on morphine-induced changes in ACTH, corticosterone and cyclic nucleotides.** Neuropharmacology (Oxford). 17(6):397-400, 1978.

The effectiveness of naloxone in blocking biochemical changes associated with morphine addiction in female rats was investigated. Concomitant administration of naloxone with morphine over a 9 day period successfully blocked the suppressive action of morphine on plasma adrenocorticotropic hormone and corticosterone, as well as the enhancing effect of morphine on cyclic guanosine monophosphate. In view of naloxone's ability to competitively block the binding of morphine at opiate receptors, it is suggested that the events leading to these biochemical changes are initiated at these sites. 21 references. (Author abstract)

002950 Hollt, Volker; Schubert, Peter. Max Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munchen 40, Germany **Demonstration of neuroleptic receptor sites in mouse brain by autoradiography.** Brain Research (Amsterdam) 151(1):149-153, 1978.

The possibility that the intracerebral distribution of receptor bound (3H)spiroperidol can be visualized by means of autoradiography was investigated. Brain slides were prepared from four male N.M.R.I. mice injected with (3H)spiroperidol and then killed. The autoradiographic evaluation of various areas of the mouse brain revealed striking regional differences in the density of silver grains. Within the densely labelled areas silver grains were seen nearly exclusively over the neuropil rather than over nerve cells. There was no indication for the presence of a considerable amount of neuroleptic binding sites outside the terminal fields of dopaminergic neurons. It was concluded that specific neuroleptic binding sites in the mouse brain were demonstrated by means of autoradiography using the potent neuroleptic drug (3H)spiroperidol. 9 references.

002951 Holmgren, Bjorn; Urba-Holmgren, Ruth; Bocar, Dem. Centro Nacional de Investigaciones Cientificas, Apartado 6990, La Habana, Cuba **Blockade of both pilocarpine and amphetamine-induced head-shaking with dopamine receptor antagonists.** Pharmacology Biochemistry and Behavior. 8(6):767-769, 1978.

The range of central dopaminergic mechanisms involved in both d-amphetamine and pilocarpine-induced head shaking was studied in 7- to 9-day-old Wistar rats by means of two dopamine antagonists: pimozide and spiroperidol. Both blocking agents exert their effects on head shaking following dose response curves which are similar, whatever the drug used to evoke head shaking. A complete blocking effect on head shaking is reached with pimozide at a dose of 2mg/kg-1 (for pilocarpine-induced head shaking) and at 0.2mg/kg-1 (for head shaking evoked by d-emphetamine). These results suggest that dopaminergic and cholinergic facilitatory influences on head shaking seem to be organized in series. 14 references. (Author abstract modified)

002952 Holmgren, Eddy; Karlsson, Jan-Olof; Sjostrand, Johan. Department of Physiology, Institute of Neurobiology, University of Goteborg, Goteborg, Sweden **Changes in synaptic function induced by blockage of axonal transport in the rabbit optic pathway.** Brain Research (Amsterdam). 157(2):267-276, 1978.

The effects of colchicine-induced inhibition of axonal transport in the retinal ganglion cells on the electrophysiological properties of the retrobulbar visual pathways were investigated in albino rabbits. Impaired signal transmission to the contralateral visual cortex, superior colliculus, and lateral geniculate body following flash light stimulation or direct optic nerve stimulation appeared 4-6 days after an intravitreous injection of 10-25mg colchicine. It is concluded that inhibition of fast axonal transport within the retinal ganglion cells interferes with transsynaptic signal transmission from optic nerve terminals in the subcortical nuclei. This indicates a functional relationship between material supplied via the rapid phase of axonal transport and unimpaired transsynaptic signal transmission. 24 references. (Author abstract modified)

002953 Hong, J. S.; Yang, H. Y. T.; Fratta, W.; Costa, E. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **Rat striatal methionine-enkephalin content after chronic treatment with cataleptogenic and noncataleptogenic antischizophrenic drugs.** Journal of Pharmacology and Experimental Therapeutics. 205(1):141-147, 1978.

The effects of chronic administration of various striatal dopamine (DA) receptor blockers on the concentrations of met-enkephalin (ME) in several rat brain regions were examined in an attempt to obtain some indication of the regulation of striatal ME containing neurons by other neuronal systems. The results show that ME content of rat striatum increases after a daily intraperitoneal treatment with haloperidol (1mg/kg/day), chlorpromazine (6mg/kg/day) or pimozide (1.5mg/kg/day) which lasts 2 weeks. A similar increase fails to occur after acute injections of haloperidol or after a 2 week treatment with clozapine (10mg/kg/day). A significant increase of ME content is obtained with 0.1mg/kg/day of haloperidol for 2 weeks; maximal responses are obtained with 1mg/kg/day. With the latter dose of haloperidol, the striatal ME content increases significantly after 7 days, but the extent of this response augments proportionally with continuation of the treatment up to 3 weeks. The results show an increase of ME content in neostriatum, globus pallidus and N. accumbens from rats injected for 2 weeks with 1 mg/kg/day of haloperidol; in contrast, the ME content of hypothalamus, septum, and medulla oblongata failed to change. Since the increase in striatal ME content was elicited by all three cataleptogenic antipsychotics studied but not by clozapine (a noncataleptogenic antipsychotic), it is suggested that the increase in striatal ME may be related to the supersensitivity of striatal DA receptors. 32 references. (Author abstract modified)

002954 Horton, R. W.; Chapman, Astrid G.; Meldrum, B. S. Dept. of Neurology, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF, England **Regional changes in cerebral GABA concentration and convulsions produced by D and by L-allylglycine.** Journal of Neurochemistry (Oxford). 30(6):1501-1504, 1978.

Regional changes in cerebral gamma-aminobutryic acid (GABA) in rats after administration of D-allylalcine and L-allylglycine were examined. In addition, d-allylglycine (3.75mM/Kg) induced convulsions characterized by repeated clonic limb movements and rapid rotation around the head to tail axis were studied. GABA concentrations were only reduced in cerebellum and pons medulla during the preconvulsive and postconvulsive periods. The localized reduction of GABA concentration is consistent with the enzymic conversion of D-allylglycine to 2-keto-4-pentenoic acid catalyzed by cerebral D-amino acid oxidase, and enzyme known to be localized to the hind brain and spinal cord. L-allyglycine (1.2mM/kg i.p.)induced convulsions in 65 to 90 min. characterised by violent running followed by tonic flexion and extension. During the preconvulsive period, GABA concentrations were reduced in all brain areas studied except the globus pallidus and ventral midbrain. The widespread decreases in GABA concentration suggest that the enzyme(s) which catalyse the conversion of L-allylglycine to 2-keto-4-pentenoic acid are widely distributed within the brain 20 references. (Author abstract modified)

002955 Howard, Joy L.; Large, Bruce T.; Wedley, Susan; Pullar, Ian A. Lilly Research Centre Erl Wood Manor, Windlesham, Surrey, England **The effects of standard neuroleptic compounds on the binding of 3H-spiroperidol in the striatum and mesolimbic system of the rat in vitro.** Life Sciences (Oxford). 23(6):599-603, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the effects of neuroleptics on 3H-spiroperidol binding in the striatum and mesolimbic system of male Wistar rats are reported. The potency of neuroleptic drugs in displacing 3H-spiroperidol binding in the striatum, but not in the mesolimbic system, paralleled their clinical potency. The ratio of activity of neuroleptic drugs in the two brain areas did not correlate with their ability to produce extrapyramidal disturbance in humans. This may be due to the interaction of neuroleptics, particularly in the mesolimbic system, with receptors not involved with in the expression of antipsychotic activity. Since the 5-hydroxytryptamine (5-HY) antagonist, cyproheptadine, inhibited the specific binding of 3H-spiroperidol in the brain, particularly in the mesolimbic area, it is suggested that 5-HT receptors may be involved in the clinical activity of neuroleptic drugs. 18 references. (Author abstract modified)

002956 Hunt, Stephen; Schmidt, Jakob. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Hills Road, Cambridge CB2 2QD, England **Some observations on the binding patterns of alpha-bungarotoxin in the central nervous system of the rat.** Brain Research (Amsterdam). 157(2):213-232, 1978.

Patterns of alpha-bungarotoxin binding were examined in the brains of Sprague-Dawley rats and compared with putative cholinergic pathways. Toxin binding sites were predominantly associated with central areas of the brain in direct receipt of sensory inputs (main and accessory olfactory bulbs, superior colliculus, ventral lateral geniculate nucleus, cochlear nuclei, substantia gelatinosa of the spinal cord and spinal trigeminal nucleus, principal sensory nucleus of the trigeminal, and dorsal column nuclei) and with limbic areas of the brain (hippocampus, amygdala, olfactory tubercle, medial mammillary nucleus, and dorsal tegmental nucleus of Gudden). Toxin did not bind to cranial motor nuclei, with the exception of the dorsal motor nucleus of the vagus and nucleus ambiguus. The inferior and accessory olivary nuclei were heavily labeled, and clusters of silver grains were distributed discretely within the granule layer of cerebellar folia I, IX, and X. In many areas of the brain, silver grains were found to overlie cell bodies, possible reflecting the presence of both membrane bound toxin and internalized ligand following initial binding to a membrane receptor site. The distribution of toxin receptors correlated reasonably well with proposed sites of cholinergic transmission within the hippocampus, interpeduncular nucleus, and cerebellum. 64 references. (Author abstract modified)

002957 Hyttel, John. Department of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500 Valby, Denmark **Effects of neuroleptics on 3H-haloperidol and 3H-cis(Z)-flupenthixol binding and on adenylate cyclase activity in vitro.** Life Sciences (Oxford). 23(6):551-555, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the effects of neuroleptics on tritiated haloperidol (3H-HAL) and cis(Z)-flupenthixol (3H-FPT) binding and on dopamine (DA) stimulated adenylate cyclase (AC) activity in male Wistar rat striatal tissue in vitro are reported. Binding studies indicated that 3H-HAL and 3H-FPT bind to striatal membranes in a saturable manner with dissociation constants of 3.1and 3.8nM, respectively. The number of bindings sites for 3H-FPT was three times higher than for 3H-HAL. Specific binding of the two ligands was highest in corpus striatum, followed by olfactory tubercles and frontal cortex. Significant 3H-FPT binding was also observed in thalamus. Neuroleptics inhibited DA stimulated AC activity and 3H-HAL and 3H-FPT binding. Butyrophenones and diphehylbutylpiperidines were weak inhibitors of 3H-FPT binding and of AC activity. A close correlation between the effects on 3H-FPT and between 3H-HAL and AC were much weaker. It is suggested that 3H-FPT binding and AC activity represent agonistic DA receptors situated postsynaptically. 15 references. (Author abstract modified)

002958 Ioffe, S.; Havlicek, V.; Friesen, H.; Chernick, V. Department of Pediatrics, University of Manitoba, Winnipeg R3E OW3, Canada **Effect of somatostatin (SRIF) and L-glutamate on neurons of the sensorimotor cortex in awake habituated rabbits.** Brain Research (Amsterdam). 153(2):414-418, 1978.

The effects of iontophoretically applied somatostatin and L-glutamate on cortical neurons in conscious adult rabbits were determined. Application of cyclic somatostatin resulted in an increase in the firing rate of spontaneously active neurons and an induction of discharges in silent neurons. Glutamate stimulation of neuronal activity was potentiated by simultaneous application of somatostatin. Discrepancies between these findings and those of previous studies are discussed. 15 references.

002959 Isaacson, Robert L.; Yongue, Brandon; Carrera, Rick. Department of Psychology, University of Florida, Gainesville, FL 32611 **Clonidine-induced body temperature changes in rats with anterior or posterior cortical damage.** Physiological Psychology. 6(2):236-240, 1978.

Long-Evans rats with anterior or posterior neocortical lesions and intact control animals were evaluated for changes in alpha-adrenergic sensitivity, as measured by the effect of the alpha-adrenergic agonist clonidine on reduction of colonic temperature. Colonic temperatures were measured after injection of .10mg/kg clonidine 4, 7, 14, 21, and 28 days after surgery. In animals with lesions in the posterior neocortex, a heightened heat loss response to clonidine was observed for 21 or more days after surgery. This exaggerated response to the drug was

not seen in rats with anterior neocortical lesions. 47 references. (Author abstract modified)

002960 Ito, S.; Nakazato, Y.; Ohga, A. Department of Pharmacology, Faculty of Veterinary Medicine, Hokkaido University, Sapporo 060, Japan **Pharmacological evidence for the involvement of Na channels in the release of catecholamines from perfused adrenal glands.** British Journal of Pharmacology (London). 62(3):359-361, 1978.

Veratridine (0.1mM) was found to be effective in producing an increase in the catecholamine output from perfused guinea pig adrenal glands in the presence of high concentrations of hexamethonium (1.83mM) and atropine (28.8microM). The response to veratridine was abolished by removal of either sodium ions or calcium ions from perfusion media and by the addition of tetrodotoxin (0.1microM). It is suggested that the response to veratridine may be due to an increase in the tetrodotoxin sensitive sodium permeability of chromaffin cell membranes. 7 references. (Author abstract)

002961 Iwata, Heitaroh; Matsuda, Toshio; Yamagami, Satoru; Hirata, Yoshihisa; Baba, Akemichi Department of Pharmacology, Faculty of Pharmaceutical Sciences, Osaka University, Osaka, Japan **Changes of taurine content in the brain tissue of barbiturate-dependent rats.** Biochemical Pharmacology. 27(15):1955-1959, 1978.

The effect of prolonged administration and abrupt withdrawal of barbital sodium on taurine content in the brains of male Sprague- Dawley rats was determined. Prolonged administration of barbital sodium caused a significant increase in cerebellar taurine content, which returned to normal soon after withdrawal of the drug. Taurine content in the cerebral cortex increased 48 hours after withdrawal. No changes in taurine content were observed in other organs. The gamma-aminobutyric acid content of the cerebral cortex and brainstem decreased significantly during barbiturate administration and returned to normal within 48 hours after drug withdrawal. A significant decrease of aspartate content in the cerebral cortex was also observed at 48 hours after withdrawal, but glutamate content did not change during or after drug administration. 29 refernces. (Author abstract modified)

002962 Jacobson, Stanley; Butters, Nelson; Tovsky, Nisa J. Department of Anatomy and Neurosurgery, Tufts University School of Medicine, Boston, MA **Afferent and efferent subcortical projections of behaviorally defined sectors of prefrontal granular cortex.** Brain Research (Amsterdam). 159(2):279-296, 1978.

Afferent and efferent subcortical projections of the midprincipalis region of rhesus monkeys were examined by injecting the retrograde tracer horseradish peroxidase (HRP) and anterograde tracers (tritiated proline, lysine, and leucine) into the sulcal cortex lining the principal sulcus. The heaviest afferents to the cortex forming the principal sulcus were from the parvocellular portions of the medial dorsal nucleus. The medical pulvinar nucleus and the nucleus limitans projected to only the anterior and posterior portions of the cortex lining the principal sucus. Projections were seen to all three cortical sectors (anterior, middle, and posterior) from the anterior, midline, intralaminar, and lateral thalamic nuclei. Although cells were seen in the hypothalamus following injections in all three sectors of the cortex lining the principal sulcus, the heaviest hypothalamic projections were noted after injections into the middle sector. HRP positive cells were found in the dorsal and lateral hypothalamic area, dorsal medial nucleus, and lateral mammillary nucleus. These findings link the midprinicpalis region with the prefrontolimbic circuit and suggest that the midprincipalis region, medial dorsal nucleus, mammillary bodies, and possibly the cingulate gyrus constitute part of an anatomical circuit concerned with memory processes. 36 references. (Author abstract modified)

002963 Jenner, P.; Clow, A.; Reavill, C.; Theodorou, A.; Marsden, C. D. University Department of Neurology, Institute of Psychiatry, and King's College Hospital Medical School, Denmark Hill, London, SE5, England **A behavioural and biochemical comparison of dopamine receptor blockage produced by haloperidol with that produced by substituted benzamide drugs.** Life Sciences (Oxford). 23(6):545-549, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the effects of haloperidol and substituted benzamide drugs on cerebral dopamine (DA) activity in mice and rats are reported. Haloperidol inhibited DA mediated behaviors (circling and stereotypy) and induced pronounced catalepsy. Metaclopramide, sulpiride, sultopride, tiapride, and clebopride also inhibited DA mediated behaviors, but only clebopride induced marked catalepsy. Haloperidol displaced 3H-haloperidol and 3H-spiperone from striatal binding sites and inhibited DA stimulated cyclase from striatal and mesolimbic regions. Substituted benzamide drugs displaced labeled ligands, but did not inhibit adenylate cyclase. Elevations of striatal homovanillic acid (HVA) produced by haloperidol and sulpiride, but not by other benzamide drugs, were partially reversed by atropine. Hypophysectomy did not prevent the elevation of forebrain HVA produced by sulpiride and metoclopramide. Substituted benzamide drugs appeared to act on cerebral DA receptors that are independent of DA sensitive adenylate cyclase and are not balanced by cholinergic input. 8 references. (Author abstract modified)

002964 Jenner, P.; Pycock, C.; Marsden, C. D.; University Department of Neurology, Institute of Psychiatry and King's College Hospital Medical School, Denmark Hill, London SE5, England **The effect of chronic administration and withdrawal of amphetamine on cerebral dopamine receptor sensitivity.** Psychopharmacology (Berlin). 58(2):131-136, 1978.

The effects of chronic administration and withdrawal of amphetamine on cerebral dopamine (DA) receptor sensitivity were investigated in male Swiss S-strain mice. Following unilateral migrostriatal lesions with 6-hydroxydopamine, the mice received d-amphetamine sulphate (2.5-20mg/kg/day) in drinking water over a period of 3 months. During this period, the circling response to apomorphine hydrochloride (0.01-0.5mg/kg) was increasingly suppressed in comparison to control animals, while spontaneous motor activity increased. The circling response to apormorphine remained suppressed 2 months after amphetamine was withdrawn. Spontaneous locomotor activity was also reduced up to 1 month after drug removal. The DA content of the lesioned side of the forebrain was 25% that of the intact side in control animals and was not further reduced by amphetamine. DA content of the intact forebrain was reduced by 43% during amphetamine administration and remained 18% depressed 1 month after drug withdrawal. No changes in 5-hydroxytryptamine or noradrenaline concentrations were observed in either the intact or lesioned side. Results indicate that chronic amphetamine treatment can induce persistent changes in dopamine receptor sensitivity either by increasing striatal receptor sensitivity or by decreasing the response of DA receptors in the nucleus accumbens. 28 references. (Author abstract modified)

002965 Jessell, T. M.; Iversen, L. L.; Cuello, A. C. Dept. of Pharmacology, Harvard Medical School, Shattuck Street, Boston, MA 02115 **Capsaicin-induced depletion of substance P from primary sensory neurons.** Brain Research (Amsterdam). 152(1):183-188, 1978.

The possibility that capsaicin-induced desensitization may be mediated by an action of the peptide substance-P containing primary afferent terminals in the substantia gelatinosa was investigated. Male Wistar rats were treated daily for 5 days with increasing subcutaneous doses of capsaicin (50, 100, 200, 200, and 400mg/kg). Radioimmunoassay and histological analysis of the brains of capsaicin treated animals, killed 10 days after the first injection, revealed a marked but incomplete loss of fluoride resistant acid phosphatase staining from substantia gelatinosa and a marked depletion of substance-P immunofluorescence from this area of dorsal horn. Naloxone displaceable (3H)diprenorphine binding and glutamic acid decarboxylase activity were not affected by capsaicin treatment in these animals. Results suggest that capsaicin produces selective and parallel depletions of fluoride resistant acid phosphatase and substance-P from the terminals of primary sensory neurons ending in the substantia gelatinosa of the spinal cord. 28 references.

002966 Jhamandas, Khem; Sawynok, Jana; Sutak, Maaja. Department of Pharmacology, Queen's University, Kingston, Ontario K7L 3N6, Canada **Antagonism of morphine action on brain acetylcholine release by methylxanthines and calcium.** European Journal of Pharmacology (Amsterdam). 49(3):309-312, 1978.

The inhibitory effect of morphine on the release of acetylcholine (ACh) from the Sprague-Dawley rat cerebral cortex was antagonized by theophylline, caffeine, and 3-isobutyl-1-methylxanthine. Theophylline antagonism of morphine action was dose related, and this agent failed to influence a comparable action of chlorpromazine on the release of ACh. Intraventricular injection of calcium also antagonized the antirelease effect of morphine. Neither methylxanthines nor calcium modified the spontaneous release of ACh in the absence of morphine. It is suggested that methylxanthine antagonism of morphine action is selective and that it could be related to the ability of methylxanthines to mobilize bound calcium. 10 references. (Author abstract)

002967 Johnston, Graham A. R. Department of Pharmacology, Australian National University, Canberra, Australia **Neuropharmacology of amino acid inhibitory transmitters.** Annual Review of Pharmacology and Toxicology. 18:269-289, 1978.

Major activities in the area of amino acid central neurotransmitters are reviewed. Primary emphasis is placed on the neuropharmacology of gamma-aminobutyric acid (GABA), which appears to be in a phase of exponential growth. The neuropharmacology of glycine, on the other hand, seems to be in a kind of lag phase, perhaps awaiting a breakthrough in the understanding of glycine metabolism. A number of widely used drugs may act, at least in part, on synaptic inhibition mediated by amino acid transmitters; these drugs include benzodiazepines, barbiturates, butyrophenones, and beta-p-chlorophenyl-GABA. Ligand binding studies are likely to become an ever increasing part of amino acid neuropharmacology and are already providing data that are difficult to obtain in any other way. 173 references. (Author abstract modified)

002968 Jones, D. G.; Devon, R. M. Department of Anatomy and Human Biology, University of Western Australia, Nedlands, WA 6009, Australia **An ultrastructural study into the effects of pentobarbitone on synaptic organization.** Brain Research (Amsterdam). 147(1):47-63, 1978.

The effects of varying doses of pentobarbitone sodium (PB) on the ultrastructure of synapses in the molecular layer of the parietal cortex were investigated in adult male rats which were unanesthetized and stunned (US), unanesthetized and cannulated (UC), or given intraperitoneal injections of PB (40, 80, 160, 300, or 400mg/kg). All material was examined qualitatively and quantitatively after aldehyde/osmium tetroxide or ethanolic phosphotungstic acid (E-PTA) treatment. In US and 160-400mg/kg PB animals, a preponderance of a variety of intraterminal profiles including synaptic vesicles, mitochondria, coated vesicles, tubular profiles, vacuoles, cisterns, and double membrane profiles was found, as well as endocytic sites over the limiting membrane of the terminal away from the cleft. Exoctotic sites along the presynaptic membrane were found in both US and UC animals. In US, UC, and 40mg/kg PB/E-PTA animals, a prominent presynaptic network was seen. Discontinuity of cleft material was found in 40-160mg/kg PB animals. PN at doses from 0-80mg/kg increased synaptic curvature negativity, while higher doses decreased negativity. Curvature negativity was accompanied by increases in synaptic length and dense projection numbers and in the perimeter and area of the presynaptic terminal. 49 references. (Author abstract modified)

002969 Jordan, C. C.; Webster, R. A. Department of Pharmacology, University College, Gower Street, London WC1E 6BT, England **The release of acetylcholine in the perfused cat spinal cord in vivo.** Neuropharmacology (Oxford). 17(6):321-327, 1978.

The central canal of the lumbosacral (L4-S1) cat spinal cord was perfused in vivo and the acetylcholine (ACh) content of the perfusate was measured by bioassay. With eserine in the perfusion fluid, electrical stimulation of the sciatic and femoral nerves increased ACh efflux. Both resting and evoked ACh efflux were increased by atropine. Substitution of the calcium content of the perfusion fluid with magnesium reduced the resting efflux and abolished the evoked efflux. Stimulation of ventral roots alone sometimes, but not always, increased the efflux of ACh, and stimulation of dorsal roots always produced a greater increase than ventral root stimulation. Although it is possible to interpret the results solely in terms of release of ACh from motoneurone collaterals, there may be additional sites of release within the spinal cord. 46 references. (Author abstract modified)

002970 Kammerer, R. Craig; Jonsson, John; Gal, Joseph; Cho, Arthur K. Dept. of Pharmacology, School of Medicine, Center for the Health Sciences, University of California, Los Angeles, CA 90024 **Use of stable isotopes in studies on the metabolism of amphetamine.** Life Sciences. 23(4):283-290, 1978.

Microsomal coincubation of 1,1,1-2H3-amphetamine and unlabeled N-hydroxyamphetamine yielded 2H-incorporation into recovered N-hydroxyamphetamine. The mole fraction of 2H in recovered phenylacetone was always close to but less than one, indicating that N-hydroxyamphetamine is not a necessary intermediate in the formation of phenylacetone. However, coincubation of 2H-labeled hydroxylamine with unlabeled 2-nitro-1-phenylpropane indicated an incorporation of 2H into both recovered nitro compound and phenylacetone. Some phenylacetone is thus formed from the nitro metabolite. Similar experiments showed phenylacetone oxime not to be a necessary intermediate in the conversion of hydroxylamine to the nitro compound. Incubation of phenyl labeled (2H) phenylacetone gave five deuterium labeled metabolites, including small quantities of labeled benzoic acid, indicating that it is a true though minor metabolite. 16 references. (Author abstract)

002971 Kan, J. P.; Malone, A.; Benedetti, M. Strolin. Centre de Recherche Delalande, 10 rue des Carrirees, F-92500 Rueil-Malmaison, France **Monoamine oxidase inhibitory properties of 5-hydroxymethyl-3-m-tolyloxazolidin-2-one (toloxatone).** Journal of Pharmacy and Pharmacology (London). 30(3):190-192, 1978.

The monoamine oxidase (MAO) inhibitory properties of 5-hydroxymethyl-3-m-tolyloxazolidin-2-one (toloxatone) were examined in rats. In vitro studies showed that toloxatone preferentially inhibits type MAO-Activity, but not as selectively as clorgyline, a known specific inhibitor of MAO-A. Findings of in vivo

experiments suggest that toloxatone possesses relatively specific type MAO-A inhibitory activity. The rate of recovery of MAO activity was correlated with the disappearance of toloxatone and its metabolites, but the extent of inhibition could not be precisely assessed. Toloxatone acts as a reversible MAO inhibitor both in vivo and in vitro and has previously been found to have antidepressant activity in animals and potential clinical efficacy in man. 11 references.

002972 Kapur, Harmash; Mottram, David R. Department of Pharmacology, School of Pharmacy, Liverpool Polytechnic, Liverpool L3 3AF, England **A comparative study on the pre- and post-synaptic alpha blocking activity of a series of benzodioxanes.** Biochemical Pharmacology (Oxford). 27(14):1879-1880, 1978.

The presynaptic and postsynaptic alpha-adrenergic blocking activity of a series of benzodioxanes were compared in the rat vas deferens. All the blockers studied exhibited a competitive type of blockade, in that the antagonists all caused a parallel shift of the clonidine dose response curve to the right. Although the postsynaptic antagonistic potencies of these agents varied over a wide range, their presynaptic potencies showed a very narrow range of activity. Results indicate that the presynaptic and postsynaptic alpha-adrenoceptors are not identical, but that a benzodioxane moiety may be important for interaction at both sites. 17 references.

002973 Kataoka, Kiyoshi; Taniguchi, Ataru; Shimizu, Hidekazu; Soda, Kenji; Okuno, Sachiko; Yajima, Haruaki; Kitagawa, Koki. Department of Physiology, Ehime University School of Medicine, Onsen-gun, Ehime 791-02, Japan **Biological activity of neurotensin and its C-terminal partial sequences.** Brain Research Bulletin. 3(5):555-557, 1978.

The hypothalamic tridecapeptide, neurotenisin, and its C-terminal partial sequences were assayed from smooth muscle contracting and blood pressure lowering properties in preparations of isolated stomach fundus, uterus, and duodenum of the rat, the isolated guinea-pig ileum, and the rabbit carotid artery. Sequences of six or more terminal amino acids produced a strong stomach fundus contracting effect, the potencies of the fragment being about equal to or slightly greater than that of the parent tridecapeptide. These fragments also elicited the ileum contracting activity, but the potencies were only one fifth to one tenth that of neurotensin. The tetrapeptide and dipeptide showed only slight stimulation in the fundus or ileum. The stimulating effect on the uterus relaxing effect on the duodenum of neurotensin were not consistent. Results suggest that the arginine or arginine-arginine residue down to the C-terminal leucine is essential for the smooth muscle contracting activity of neurotensin, while full length sequence may be needed for the hypotensive effect. 15 references. (Author abstract modified)

002974 Kawakami, Masazumi; Sakuma, Yasuo; Akema, Tatsuo. Department of Physiology, Yokohama City University School of Medicine, Yokohama, Japan **Effects of estrogen and aminergic drugs on thresholds of medial basal hypothalamic axons in the median eminence of the rat.** Brain Research (Amsterdam). 151(3):533-544, 1978.

Antidromic responses were induced in the medial basal hypothalamus (MBH) of female Wistar rats by median eminence (ME) stimulation, and thresholds were measured under various endocrine conditions. In 83 out of 97 responses, repetitive shocks to the ME at 2-40Hz induced a fractionation of antidromically driven spikes into two components. In the remainder, the antidromically activated spikes were stable to stimulation at high frequency. Both types of response tended to show higher threshold values in proestrus than in diestrus. Application of conditioning electrical shocks to the ME decreased the threshold in the fractionating spikes for successive test pulses. Effects of conditioning persisted in animals with chronic complete deafferentation of the MBH but were abolished in intact rats by reserpine treatment. Dopamine, but not norepinephrine or serotonin, applied to the ME mimicked the threshold decreasing effect of conditioning on fractionating spikes. Results suggest the possibility of some dopaminergic neural mechanism projecting from the MBH to the ME and acting on the axons of a particular type of MBH neuron characterized by fractionating spikes. 33 references. (Author abstract modified)

002975 Kempf, E.; Zwiller, J.; Gill, M.; Mack, G.; Mandel, P. Centre de Neurochimie du CNRS, Faculte de Medecine, F-67085 Strasbourg Cedex, France **Effect of acute morphine administration on the cerebellar cyclic GMP level in two strains of mice.** Communications in Psychopharmacology. 2(2):85-91, 1978.

To investigate the involvement of genetic factors contributing to the effect of morphine on the cerebellar cyclic guanosine monophosphate (CGMP) system in two strains of mice, C57 and DBA, which differ in their motor response to this opiate, male mice were injected with morphine (20mg/kg) intraperitoneally and sacrificed 30 min after the injection. No significant differences in the levels of cGMP were observed between the control animals of the two strains. It is noted that morphine produces a 64% decrease in the cGMP content of cerebellum in the DBA mice as well as a lowing of motor activity. In both strains the enzyme activities, guanylate cyclase and phosphodiesterase, are unchanged after morphine injection. 16 references. (Author abstract modified)

002976 Kennedy, Lois Ann. University of Manitoba, Canada **Teratological evaluation of ethanol, pentobarbital, and combinations of these, in the rat.** Dissertation Abstracts International. 38(12):5835-B, 1978.

The teratogenicity of short-term intoxication was investigated in pregnant rats who were treated with three doses of ethanol, three doses of pentobarbital, or combinations of these, on days 9 through 12 of gestation. Treatment with ethanol was associated with a reduction in placental weight; gestational intoxication with either ethanol or pentobarbital was associated with a temporary reduction in maternal weight gain, but no significant difference in weight or length of the offspring at term. Although pathological changes were observed in the liver and kidney of ethanol treated mothers, such changes were not evident in the corresponding fetal tissues. With the exception of minor changes in the maternal kidney, and a nonspecific stimulation of the reticulo-endothelial system, microscopic examination of the fetal and maternal tissues revealed no changes following short-term intoxication with pentobarbital. In pregnant animals treated simultaneously with ethanol and pentobarbital, no consistent pattern of response in the parameters evaluated is reported. It is suggested that placental and ovarian function should be carefully monitored in human pregnancies involving maternal alcohol abuse. (Journal abstract modified)

002977 Khayyal, M. T.; Samaan, H. A.; Galal, E. E. Department of Pharmacology, Faculty of Pharmacy, Cairo University, Cairo, Egypt **The antagonism of the analgesic effect of dipyrone by L-dopa and its relation to brain amine concentrations.** Journal of Pharmacy and Pharmacology (London). 30(3):195-196, 1978.

The analgesic effect of dipyrone and its antagonism by L-dopa were examined in relation to brain concentrations of norepinephrine (NE) and 5-hydroxytryptamine (5-HT). Hotplate reaction times (HPRT) were determined in five groups of 30 Swiss Albino mice each given saline, dipyrone (90mg/kg and 450mg/kg by mouth), L-dopa (100mg/kg, i. p.), and dipyrone

(90mg/kg) and L-dopa in combination. Brain concentrations of NE and 5-HT were analyzed in five additional groups of mice given the same drug regimens. The oral median analgesic dose of dipyrone was 90mg/kg in the hotplate test at 55 degrees. L-dopa alone induced a transient increase in HPRT 30 minutes after injection. Dipyrone alone induced marked analgesia that was maintained over 90 minutes. Dipyrone given simultaneously with L-dopa induced significant analgesia maintained for 30 minutes. The dipyrone analgesia was correlated with the drug's effect on the brain ratio of 5-HT to NE rather than with its effects on the brain concentration of either amine. The higher dose of dipyrone caused a greater rise in 5-HT concentration and consequently in the 5-HT to NE ratio; the concomitant administration of L-dopa lowered this ratio and returned the animals' sensitivity to thermal stimuli to normal levels. 14 references.

002978 King, Stephen; Phillips, Allen T. Dept. of Biochemistry and Biophysics, Pennsylvania State University, University Park, PA 16802 **Aromatic aminotransferase activity of rat brain cytoplasmic and mitochondrial aspartate aminotransferases.** Journal of Neurochemistry (Oxford). 30(6):1399-1407, 1978.

Mitochondrial and cytoplasmic forms of aspartate aminotransferase were purified from rat brain homogenates and tested for their ability to catalyze transamination of various aromatic amino acids. The mitochondrial enzyme exhibited acitivity toward tyrosine and phenylalanine with 2-oxoglutarate as acceptor, although the specific activities were less than 1% of the corresponding aspartate activity when all substrates were 10 mM. Even less activity was seen with DOPA, 5-hydroxytryptophan and tryptophan. The cytoplasmic aspartate aminotransferase was active toward tryptophan, 5-hydroxytryptophan, and DOPA, but these transaminations were favored by pyruvate or oxaloacetate rather than 2-oxoglutarate as keto acid. Based on co migration of aromatic activities with the respective aspartate aminotransferases during isoelectric focusing and based on equal sensitivities of aromatic transamination and aspartate transamination to inhibition by vinylglycine, it is concluded that all activities reside in the aspartate aminotransferase enzymes. Some doubt exists, however, as to the physiological significance of these alternate activities in view of the requirement that aromatic amino acids must compete with aspartate for transaminatin by these enzymes. 20 references. (Author abstract)

002979 Kostowski, W.; Jerlicz, Maria; Bidzinski, A.; Hauptmann, Miroslawa. Department of Pharmacology and Physiology of the Nervous System, Psychoneurological Institute, 02-957 Warsaw, Poland **Studies on the effect of lesions of the ventral noradrenergic tract on the antinociceptive action of morphine.** Psychopharmacology (Berlin). 57(2):189-192, 1978.

Lesions were made in the ventral tegmental noradrenergic tract (VT) in male Wistar rats; in some animals, the lesions also involved the dorsal tegmental noradrenergic tract (DT). Morphine analgesia was examined by the tail compression method 8 or 9 days after the lesions. VT lesions produced no changes in morphine activity, while lesions involving both VT and DT produced a partial attenuation of the antinociceptive action of morphine. Results suggest that the ascending noradrenergic fibers forming the VT are not essential for the antinociceptive effect of morphine. 37 references. (Author abstract)

002980 Kostrzewa, Richard M.; Klara, Joan W.; Robertson, James; Walker, Lary C. Department of Pharmacology, East Tennessee State University, Johnson City, TN 37601 **Studies on the mechanism of sprouting of noradrenergic terminals in rat and mouse cerebellum after neonatal 6-hydroxydopa.** Brain Research Bulletin. 3(5):525-531, 1978.

The neurotoxin 6-hydroxydopa (6-OHDOPA), given to Sprague-Dawley rats at birth, caused a 46% reduction at 5 weeks of age in tyrosine hydroxylase activity in the locus coeruleus, the nucleus of origin for noradrenergic fibers innervating the cerebellum. However, neonatal 6-OHDA also elevated tyrosine hydroxylase activity and norepineprhine (NE) content by 50% in the cerebellum. By treating pregnant mice with 6-OHDOPA at different stages of gestation, a dissociation between the elevated cerebellar NE levels and reduced telencephalic NE levels was demonstrated. Acute treatment with amphetamine, metaraminol, apomorphine, alpha-methyl-p-tyrosine, L-dihydroxyphenylalanine, or tyramine at birth failed to produce a permanent elevation in cerebellar NE content. It is concluded that alteration of the telencephalic noradrenergic fibers is not a ncessary event for the initiation of sprouting of noradrenergic fibers in the cerebellum. Since none of the acute acting pharmacological agents caused a permanent elevation of NE in the cerebellum, it appears that damage, and not simple stimulation of or blockade, is a necessary event for the initiation of sprouting. 48 references. (Author abstract modified)

002981 Krogsgaard-Larsen, P.; Johnston G. A. R. Dept. of Chemistry BC, Royal Danish School of Pharmacy, Copenhagen, Denmark **Structure-activity studies on the inhibition of GABA binding to rat brain membranes by muscimol and related compounds.** Journal of Neurochemistry (Oxford). 30(6):1377-1382, 1978.

A series of compounds structurally related to muscimol (5-aminomethyl-3-isoxazolol) were tested as inhibitors of the sodium independent binding of GABA to membranes from rat brain. Muscimol, 5-(1-aminoethyl)-3-isoxazolol, 5-(2-aminoethyl)-3-isoxazolol (homomuscimol), and the bicyclic derivative 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-o1 (THIP) were relatively potent inhibitors of GABA binding. THIP is an analogue of muscimol locked in a folded conformation. The structurally related compound 1,2,3,6-tetrahydropyridine-4-carboxylic acid (isoguvacine), a semirigid analogue of trans-4-aminocrotonic acid, was also a potent inhibitor of GABA binding. Apart from muscimol, these inhibitors of GABA binding did not influence the sodium dependent, high affinity uptake of GABA in rat brain slices, whereas the potent GABA uptake inhibitors guvacine and nipecotic acid did not influence GABA binding. Results support previous findings that different conformational modes of GABA interact with GABA postsynaptic receptors and the neuronal GABA transport system in rat brain, and indicate that the active conformation of GABA with respect to the receptors is partially folded and almost planar. Based on a comparison of the present results with previous in vivo studies the structural requirements for GABA-like activity in rat cerebral cortex and cat spinal cord seem to be somewhat different. 34 references. (Author abstract)

002982 Krstic, M. K.; Djurkovic, Draginja. Department of Pharmacology, Faculty of Medicine, P. O. Box 662, 11000 Beograd, Yugoslavia **Cardiovascular response to intracerebroventricular administration of acetylcholine in rats.** Neuropharmacology (Oxford). 17(6):341-347, 1978.

General characteristics of the cardiovascular response to intracerebroventricular (ICV) injection of acetylcholine (ACh) and the mechanisms mediating this response in rats were studied. ACh produced a pressor response which was sometimes followed by a prolonged depressor response. The vascular response to ACh was generally not accompanied by marked changes in heartrate. The pressor effect of ACh was abolished after transsection of the spinal cord, ICV administration of atropine or nicotine, and intravenous (i.v.)administration of phenoxybenzamine, tolazoline, or methylatropine. The pressor response to ACh was reduced after bilateral adrenalectomy or i.v. injec-

tion of bretylium but was not affected by bilateral cutting of the vagosympathetic trunks and ICV or i.v. administration of hexamethonium. It is concluded that the pressor effect of ACh results from the activation of the central muscarinic receptor sites, which evokes the activation of the muscarinic receptors in the sympathetic ganglia and the adrenal medulla followed by the release of catecholamines from adrenergic nerve terminals and the adrenal medulla. 30 references. (Author abstract modified)

002983 Kuhn, Donald M.; Shah, Nandkumar S. Section on Biochemical Pharmacology, National Heart, Lung, and Blood Institute, NIH, Bethesda, MD 20014 **Subcellular localization of (14C)methaqualone in mouse brain: effects of hepatic microsomal enzyme inhibition.** Toxicology and Applied Pharmacology. 46(1):109-116, 1978.

The subcellular distribution of radiolabeled methaqualone (14C-MTQ) in brain and the effects of the hepatic microsomal enzyme inhibitor SKF-525-A on the concentrations and distribution of 14C-MTQ were investigated in female Swiss-Webster mice. In plasma and brain, peak concentrations occurred 1.5hours after oral administration of 25mg/kg 14C-MTQ; approximately 0.11% of the administered dose appeared in the brain. Pretreatment with SKF-525-A markedly enhanced plasma and brain MTQ levels up to 12 hours. MTQ levels at 24 hours were negligible. A major proportion (67-81%) of the 14C-MTQ was recovered in the soluble cytoplasm. Of the particulate fractions, the myelin contained the highest concentration (11-20%), followed by the nuclear fraction (2-7%). Only small amounts of 14C-MTQ were detected in synaptosomes, membrane fragments, mitochondria, and microsomes. It is concluded that MTQ is not specifically bound to nuclei, mitochondria, and microsomes and that the presence of higher amounts in the myelin fraction is due to its lipophilic property. 37 references. (Author abstract modified)

002984 Kuriyama, Kinya; Yoneda, Yukio. Department of Pharmacology, Kyoto Prefectural University of Medicine, Kamikyo-Ku, Kyoto 602, Japan **Morphine-induced alterations of gamma-aminobutyric acid and taurine contents and L-glutamate decarboxylase activity in rat spinal cord and thalamus: possible correlates with analgesic action of morphine.** Brain Research (Amsterdam). 148(1):163-179, 1978.

The effects of chronic or acute morphine administration on gamma-aminobutyric acid (GABA) and taurine levels and L-glutamate decarboxylase (GAD) activity in rat spinal cord and thalamus were examined. Acute administration of morphine induced significant increases of GABA content and GAD activity at the dorsal parts of the dorsal horn and surroundings of the central canal in the spinal cord. In the thalamus, acute morphine administration also induced singificant increases of GABA content and GAD activity in the vicinity of the ventrolateral part of the ventral nucleus (VM), entopeduncular nucleus, nucleus reuniens thalami, nucleus parafascicularis thalami (PF), and intepeduncular nucleus. GABA increased most significantly in the VM and PF and did not change in the periaqueductal gray matter. Microdistribution of taurine in the spinal cord and thalamus was not altered by acute morphine administration. Chronic morphine treatment, by contrast, resulted in significant increases in taurine content in the spinal cord but no change in GABA content of spinal cord or thalamus. Results suggest that morphine analgesia may involve mechanisms intensifying the inputs of GABA inhibitory neurons at the levels of spinal cord and thalamus. 28 references. (Author abstract modified)

002985 Laduron, P. M.; Janssen, P. F. M.; Leysen, J. E. Department of Biochemical Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse,Belgium **Characterization of specific in vivo binding of neuroleptic drugs in rat brain.** Life Sciences (Oxford). 23(6):581-585, 1978.

In a paper presented at the Janssen Symposium on Receptors of dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, characteristics of specific in vivo binding of neuroleptic drugs in Wistar rat brain are reported. In vivo binding of 3H-spiperone was saturable in the striatum, limbic system, and frontal cortex, but not in the cerebellum. Nonspecific binding was different in all brain regions; thus, the amount of labeling in the cerebellum is not an appropriate blank value (nonspecific binding) for other regions. Tritiated spiperone binding revealed a specific subcellular distribution only when a very low dose was injected into rats. Ex vivo studies of the relative affinities of pimozide, pipamperone, and spiperone for dopamine and serotonin receptors were also carried out. Profiles of the three drugs in the limbic system occupied an intermediary position between the striatum and frontal cortex, indicating that both dopaminergic and serotonergic receptors are present in this brain area. 9 references. (Author abstract modified)

002986 Lahti, Robert A.; Collins, R. James. Upjohn Company, Kalamazoo, MI 49001 **Chronic naloxone results in prolonged increases in opiate binding sites in brain.** European Journal of Pharmacology (Amsterdam). 51(2):185-186, 1978.

The effects of chronic naloxone on opiate binding parameters were investigated in Sprague-Dawley rats given saline or naloxone (10mg/kg/day) infusions for 4 weeks. Analysis of the 3H-naloxone binding data from these animals showed that the increase in 3H-naloxone binding resulting from chronic naloxone treatment was due to an increase in the number of receptors, with no change in the affinity constants; the number of binding sites increased by 40% from 192 to 269fmoles/mg protein, while the dissociation constants remained unchanged at 2.58 and 2.78nM, respectively, for saline and naloxone treated rats. The change in receptor number was apparent 7 days after cessation of naloxolone treatment. These results indicate that the supersensitivity to morphine seen after chronic naloxone treatment is correlated with an increase in the number of binding sites, which may be a mechanism to overcome chronic receptor blockage. 4 references.

002987 Lambert, Geoffrey A.; Lang, William J.; Friedman, Eitan; Meller, Emanuel; Gershon, Samuel. Neuropsychopharmacology Research Unit, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Pharmacological and biochemical properties of isomeric yohimbine alkaloids.** European Journal of Pharmacology (Amsterdam). 49(1):39-48, 1978.

The stereochemical and pharmacological properties of yohimbine and some of its isomers were investigated. Several pharmacological and physical properties of a selection of the isomers have been determined with a view to elucidating which might be important in the elaboration of their known behavioral effects. Activity was not dependent upon lipid solubility or on the ease of access to the central nervous system. The isomers were found to be weak inhibitors of rat brain acetylcholinesterase and weak antagonists at muscarinic cholinergic receptors. In the rat brain in vitro they did not possess significant monoamine oxidase inhibiting properties nor did they inhibit the uptake of serotonin. The isomers were revealed to be relatively potent antagonists of 5HT on the rat isolated fundus preparation and their potency in this preparation may be related to their ability to produce behavioral and cardiovascular effects in man and dogs. 44 references. (Author abstract)

002988 Lomax, P.; Ary, Marylouise; Sorensen, S. M. Department of Pharmacology, School of Medicine, University of Cali-

fornia, Los Angeles, CA 90024 **Dopamine-induced hypothermia in morphine-dependent rats.** Neuropharmacology (Oxford). 17(11):971-974, 1978.

The effect of lateral ventricular injection of dopamine (DA) on body temperature was investigated in normal and morphine dependent male Sprague-Dawley rats. DA induced a significantly greater hypothermic response in animals of the morphine dependent group than in controls when injected 72 hours after implantation of a subcutaneous morphine pellet. The increased sensitivity of the morphine dependent animals is probably the result of changes at the dopaminergic synapse. The possibility that this effect is due to an increase in receptor sensitivity or to an increase in the number of receptors as a result of presynaptic inhibition of transmitter release is discussed. 37 references. (Author abstract modified)

002989 Loonen, Anton J.M.; Van Wijngaarden, Ineke; Janssen, Paul A.J.; Soudijn, Willem. Department of Pharmaceutical Chemistry, University of Amsterdam, Plantage Muidergracht, 24, Amsterdam, The Netherlands **Regional localization of halopemide, a new psychotropic agent, in the rat brain.** European Journal cf Pharmacology (Amsterdam). 50(4):403-408, 1978.

The uptake, regional localization, and subcellular distribution of halopemide, a new psychotropic agent, were investigated in male Wistar rats. The concentration of halopemide was about 10 times less than that of its chemical congener R-29800 and of spiperone in rat brain 1 hour after subcutaneous injection of the druges, but levels of the three compounds in pituitary gland were the same. The distribution profile of halopemide in rat brain differs from that of neuroleptics; the highest level of halopemide was found in septal and thalamic areas, whereas neuroleptics are concentrated in the caudate nucleus, nucleus accumbens, and tuberculum olfactorium. Subcellular distribution experiments showed that halopemide was far less particle bound than neuroleptics in the caudate nucleus. 7 references. (Author abstract modified)

002990 Lucchelli, A.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Stratial content of Ca2-dependent regulator protein and dopaminergic receptor function.** Brain Research (Amsterdam). 155(1):130-135, 1978.

To enchance understanding of the role of Ca2 dependent regulator (CDR) protein in dopamine (DA) receptor function, the effects of denervation were examined. The striatal CDR content following the degeneration of striatal DA axon terminals elicited by a brain hemitransection was measured in male Sprague-Dawley rats. Results indicate that the CDR increase is strictly related to the DA receptor supersensitivity which is elicited in striatum by both chronic haloperidol or hemitransection. Neither a single injection of haloperidol which blocks DA receptors nor repeated doses of apomorphine which stimulate DA receptors change the CDR content of the striatal pellet. CDR increases were observed in striatum but not in nucleus accumbens or frontal cortex. 27 references.

002991 Lundh, Hakan. Department of Pharmacology, University of Lund, Lund, Sweden **Effects of 4-aminopyridine on neuromuscular transmission.** Brain Research (Amsterdam). 153(2):307-318, 1978.

The effects of 4-aminopyridine (4-AP) on neuromuscular transmission were investigated in vitro in the neuromuscular junction of the extensor digitorum longus muscle of male Sprague-Dawley rats and in the frog (Rana temporaria) sartorius muscle. The drug powerfully increased transmitter release from motor nerve terminals in response to single nerve impulses. The drug also enhanced transmitter release during repetitive nerve activity, but at D-tubocurarine blocked endplates, only the first impulses caused increased transmitter release at stimulation frequencies at or above 50Hz. At magnesium and botulinum poisoned endplates, 4-AP potentiated transmitter release at every stimulus during tetanic nerve stimulation and restored neuromuscular transmission. Spontaneous transmitter release in the rat was not affected by the drug, but at some frog endplates miniature endplate potential frequency increased. Studies of the mode of action of 4-AP suggest that the drug increases transmitter release by enhancing the influx of calcium ions during depolarization of the nerve terminal. 23 references. (Author abstract modified)

002992 Lynch, Marina A.; Leonard, B. E. Pharmacology Department, University College, Galway, Republic of Ireland **Changes in brain gamma-aminobutyric acid concentrations following acute and chronic amphetamine administration and during post amphetamine depression.** Biochemical Pharmacology (Oxford). 27(14);1853-1855, 1978.

The effects of acute and chronic amphetamine administration of gamma-aminobutyric acid (GABA) in those regions in which changes in brain monoamines are known to occur was studied in male Wistar rats. The acute administration of d-amphetamine caused an increase in the GABA content of the brainstem and thalamus. Acute chloropromazine treatment lowered the GABA concentration in the thalamus, olfactory lobes, and brainstem. Although this neuroleptic antagonized the stereotypy induced by amphetamine, the drug combination markedly increased the GABA content of all brain regions studied. Following chronic administration of amphetamine for 2 weeks, the GABA content of striatum and thalamus decreased, even though the stereotyped behavior was more marked than that occurring after acute amphetamine administration. During the period of postamphetamine depression, the GABA content of the striatum and brainstem were also decreased, whereas that of the amygdala was increased. Although the changes in GABA content did not reflect changes in gross behavior following amphetamine administration, these results suggest that GABA may play an ancillary role in determining the neuropharmacological profile of amphetamine. 15 references. (Author abstract)

002993 Mailman, R. B.; Mueller, R. A.; Breese, G. R. Biological Sciences Research Center, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **The effect of drugs which alter GABA-ergic function on cerebellar guanosine-3',5'-monophosphate content.** Life Sciences (Oxford). 23(6):623-627, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Atagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the effects of drugs that interact with gamma-aminobutyric acid (GABA) or dopamine (DA) containing neurons on cerebellar guanosine-3',5'-monophosphate (cGMP) content in male Sprague-Dawley rats are reported. Cerebellar cGMP was increased by picrotoxin and thyrotropin releasing hormone and decreased by ethanol and diazepam. Baclofen and gama-hydroxybutyrate (GHB) had no significant effect on cGMP at doses that caused behavioral changes. Apomorphine raised and haloperidol lowered cerebellar cGMP. Apomorphine-induced increases in cGMP were blocked by haloperidol, but not by GHB or baclofen given 8 minutes before sacrifice. However, baclofen given 1 hour before sacrifice caused effects similar to those of haloperidol. Results are discussed in terms of interactions of DA and GABA containing neurons. 20 references. (Author abstract modified)

002994 Malthe-Sorenssen, D.; Wood, P. L.; Cheney, D. L.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Modulation of**

the turnover rate of acetylocholine in rat brain by intraventricular injections of thyrotropin-releasing hormone, somatostatin, neurotensin and angiotensin II. Journal of Neurochemistry (Oxford). 31(3):685-691, 1978.

The turnover rate of acetylcholine (ACh-TR) was measured in frontal and parietal cortices, striatum, hippocampus, diencephalon, and brainstem of male Sprague-Dawley rats, following intraventricular injection of tyrotropin-releasing hormone (TRH), somatostatin, neurotensin, and angiotensin II. TRH increased ACh-TR in parietal but not in frontal cortex, whereas somatostatin, neurotensin, and angiotensin II failed to change ACh-TR in these cortical areas. Somatostatin and neurotensin increased ACh-TR in diencephalon, but TRH and angiotensin II did not. All four peptides decreased ACh content in parietal cortex but not in frontal coretex. Only somatostatin changed the ACh-TR in pons medulla. Larger doses of TRH, neurotensin, and angiotensin II did not elicit greater or more general changes in ACh-TR, but high doses of somatostatin increased the ACh-TR in hippocampus and induced barrel rotation. Intraseptal injections of somatostatin induced a long-lasting catalepsy but did not change hippocampal ACh-TR or elicit barrel rotation. The synthetic peptides L-prolylglycine, poly-L-proline, and poly-L-glutamate had no effect on ACh-TR. 50 references. (Author abstract modified)

002995 Marangos, P. J.; Paul, S. M.; Greenlaw, P.; Goodwin, F. K.; Skolnick, P. NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Demonstration of an endogenous, competitive inhibitor(s) of (3H) diazepam binding in bovine brain.** Life Sciences. 22(21):1893-1900, 1978.

An endogenous inhibitor (or inhibitors) of (3H)diazepam binding to synaptosomes was demonstrated in bovine brain. The inhibitory activity of crude extracts was heat stable, dialyzable, and not affected by ether extraction. Three distinct peaks of inhibitory activity were resolved using Sephadex G-25 chromatography. The lowest molecular weight peak (less than 700 daltons) had the highest specific inhibitory activity, and its inhibition of (3H)diazepam binding was competitive. This fraction appears to be unique to brain, since similar low molecular weight fractions were not observed in muscle or liver. Thin layer chromatography revealed a discrete band of inhibitory activity in the two low molecular weight peaks. 11 references. (Author abstract modified)

002996 Marco, E.; Mao, C. C.; Revuelta, A.; Peralta, E.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Turnover rates of gamma-aminobutyric acid in substantia nigra, N. caudatus, globus pallidus and N. accumbens of rats injected with cataleptogenic and non-cataleptogenic antipsychotics.** Neuropharmacology (Oxford). 17(8):589-596, 1978.

The turnover rates of gamma-aminobutyric acid (TR/GABA) were measured in the substantia nigra, caudate nucleus, globus pallidus, and nucleus accumbens of male Sprague-Dawley rats injected intraperitoneally with a single dose of haloperidol, pimozide, chlorpromazine, clozapine, and thioridazine. The cataleptogenic antipsychotics, haloperidol (1.3or 4mcmole/kg), pimozide (3mcmole/kg), and chlorpromazine (18mcmole/kg), increased TR/GABA in the nucleus accumbens and globus pallidus, but failed to change that in the substantia nigra and caudate nucleus. The noncataleptogenic clozapine (30mcmole/kg) and thiridazine (50mcmole/kg) increased TR/GABA in all four areas. TR/GABA in the nucleus accumbens was increased by d-butaclamol (2.6mcmole/kg) but not by l-butaclamol. Chronically administered haloperidol (4mcmole/kg, twice daily for 7 days) and clozapine (30mcmole/kg, twice daily for 7 days) increased TR/GABA in the nucleus accumbens but not in the globus pallidus. Results suggest that the increase of TR/GABA in the nucleus accumbens may be associated with the therapeutic action of antipsychotics, since this response failed to show tolerance. 38 references. (Author abstract modified)

002997 Marigold, Julia; Taberner, Peter V. Department of Pharmacology, University of Bristol, University Walk, Bristol, BS8 1TD, England **The effects of allyglycine on GABA synthesis in vivo.** Biochemical Pharmacology (Oxford). 27(8):1109-1112, 1978.

The relative incorporation of 14C into gamma-aminobutyric acid (GABA) and glutamate following the intracerebroventricular injection of D-(U-14C) glucose was determined in adult female LACG mice pretreated with either 2mM/kg intraperitoneal allyglycine or saline. The proportion of total counts appearing in glutamate declined slightly between 1 and 3 hours postinjection, but the proportion of total counts in GABA decreased significantly from control over the same period. There was a strong positive correlation between the ratio of counts in GABA to glutamate and the time after injection of allyglycine. A significant fall in the specific activity of GABA was observed from 1 hour postinjection of allyglycine onwards. These effects preceded the convulsions induced by allyglycine by at least 1 to 1.5hours, but the maximal effect was observed at the onset of convulsions at 2.5to 3 hours. These results support the view that the convulsant actions of allyglycine or its deaminated metabolite are due to the inhibition of glutamate decarboxylase and consequent reduction in GABA synthesis. 20 references. (Author abstract)

002998 Markstein, R., Herrling, P. L.; Burki, H. R.; Asper, H.; Ruch, W. Biological and Medical Research, Sandoz Ltd., CH-4002 Basel, Switzerland **The effect of bromocriptine on rat striatal adenylate cyclase and rat brain monoamine metabolism.** Journal of Neurochemistry (Oxford). 31(5):1163-1172, 1978.

The effects of bromocriptine on central monoamine metabolism and on dopamine (DA) sensitive adenylate cyclase were investigated in slices and homogenates from male RAC rat striatum. In marked contrast to DA, norepinephrine (NA), and apomorphine, bromocriptine had no stimulatory effect on adenylate cylase activity but antagonized the stimulatory effects of NA and DA. Bromocriptine (10mg/kg, subcutaneoulsy) decreased the turnover of DA in striatum and limbic structures 3 hours after drug administration, but increased NA turnover in the brainstem and 5-hydroxytryptamine turnover in the cortex 4 hours after treatment. Possible modes of action of bromocriptine are discussed. 45 references. (Author abstract modified)

002999 Marquardt, Gerald M.; DiStefano, Victor; Ling, Lydia L. Environmental Protection Agency, Metabolic Effects Branch, OPP/CED, 401 M Street S.W., Washinton, DC 20460 **Effects of racemic, (S)- and (R)-methylenedioxyamphetamine on synaptosomal uptake and release of tritiated norepinephrine.** Biochemical Pharmacology (Oxford). 27(10):1497-1502, 1978.

The actions of (plus or minus)-, (S-) and (R)-methylenedioxyamphetamine (MDA) on the uptake and release of (3H)norepinephrine (NE) in synaptosomal preparations were examined to determine whether differential effects of (plus or minus)-, (S)- and (R)-MDA could be observed. Racemic, (S)-, and (R)-MDA were potent competitive inhibitors of (3H)norepinephrine (NE) uptake in hypothalamic synaptosomes from male Sprague-Dawley rats. (S)- and (R)-alpha-methyldopamine were the most potent competitive inhibitors of brain (3H)NE uptake reported to date. Racemic, (S)-, and (R)-MDA were slightly less potent as releasing agents than (plus or minus), (), and(-)amphetamine, respectively. (S)- and (R)-alpha-

methyldopamine were the most potent releasing agents. examined. 15 references. (Author abstract modified)

003000 Marquardt, Gerald M; DiStefano, Victor, Ling, Lydia L. Environmental Protection Agency, Metabolic Effects Branch, OPP/CED, 401 M Street S.W., Washington, DC 20460 **Metabolism of beta-3,4-methylenedioxyamphetamine in the rat.** Biochemical Pharmacology (Oxford). 27(10):1503-1505, 1978.

The metabolites of beta-3,4-methylenedioxyamphetamine (MDA) enantiomers were determined in the urine and brains of male Sprague-Dawley rats treated with (3H)MDA. Unchanged (3H)MDA represented the majority of urine tritium 2 hours after drug treatment, while 3-0-methyl-alpha-dopamine and its glucoronide conjugate accounted for the majority of urine radioactivity at 6, 16, and 24 hours after treatment. In brain the majority of radioactivity 30-60 minutes after dosing was in the form of MDA. Analysis of brain samples 6-24 hours after dosing, however, revealed that free alpha-methyldopamine accounted for the majority of brain radioactivity. 9 references.

003001 Martin, I. L.; Baker, G. B.; Mitchell, P. R. Medical Research Council Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **The effect of viloxazine hydrochloride on the transport of noradrenaline, dopamine, 5-hydroxytryptamine and gamma-amino-butyric acid in rat brain tissue.** Neuropharmacology (Oxford). 17(6):421-423, 1978.

The effects of viloxazine on the uptake, basal release and potassium-induced release of noradrenaline (NE), dopamine (DA), 5-hydroxytryptamine (5-HT), and gamma-aminobutyric acid (GABA) were examined in rat brain. Viloxazine caused marked inhibition of NE uptake in the hypothalamus and a weaker inhibition of 5-HT uptake in the striatum. The drug had no effect on the uptake of DA or GABA. Viloxazine caused the release of 5-HT from a striatal tissue preparation but had no effect on the release of NE, DA, or GABA. Viloxazine did not appear to facilitate or inhibit the potassium-induced release of any of the neurotransmitters studied. 10 references.

003002 Martin, I. L.; Candy, J. M. MRC Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **Facilitation of benzodiazepine binding by sodium chloride and GABA.** Neuropharmacology (Oxford). 17(11):993-998, 1978.

Gamma-aminobutyric acid (GABA) facilitated benzodiazepine binding in male Wistar rat brain membrane fragments. The binding facilitation produced by GABA obeyed Michaelis-Menten kinetics; Scatchard analysis revealed that this facilitation was due to an increased affinity of the benzodiazepine receptor. Sodium chloride itself increased benzodiazepine binding and also markedly enhanced the facilitation caused by GABA, by a further increase in the affinity of the benzodiazepine receptor. The enhancement of the GABA effect produced by sodium chloride showed sigmoidal kinetics indicating cooperativity, but no evidence was found for the involvement of sodium dependent GABA binding in this interaction. 14 references. (Author abstract modified)

003003 Massari, V. John; Tizabi, Yousef; Jacobowitz, David. Department of Pharmacology, Howard University College of Medicine, Washington, DC 20059 **Evaluation of the effect of p-chloroamphetamine on individual catecholaminergic nuclei in the rat brain.** European Journal of Pharmacology (Amsterdam). 50(3):279-282, 1978.

Short-and long-term effects of p-chloroamphetamine (PCA) on levels of catecholamines (CA) in discrete CA cell body and axon terminal areas were investigated in male Sprague-Dawley rats. The CA levels were unaffected, except for a transient fall in dopamine in the arcuate nucleus. The results do not support the suggestion that PCA is neurotoxic to CA cells. 11 references. (Author abstract)

003004 Matsuzaki, M.; Misra, A. L. Nippon Merck-Banyu Research Institute, Okazaki City, Japan **Cocaine and pseudococaine: comparative effects on electrical after-discharge in the limbic system of cats.** Brain Research Bulletin. 3(4):341-347, 1978.

The effects of cocaine and its dextroisomer pseudococaine on electrical after-discharge (AD) evoked by electrical stimulation of the hippocampus or amygdala were studied in four cats with electrodes implanted in the brain. Intravenous injection of cocaine produced a suppressive effect on the AD while producing low voltage fast waves in the electrical activities of the brain associated with behavioral excitation. In contrast, pseudococaine at the same dose as cocaine failed to show a significant suppressive effect on the AD except at high doses. Pseudococaine produced high voltage slow waves in the EEG associated with behavioral depression. A linear dose response relationship was observed for the suppressive effect of cocaine on the AD. The results suggest that the limbic system may be involved as a primary site of action of cocaine in the central nervous system. 23 references. (Author abstract)

003005 Max, Stephen R.; Schwab, Martin; Dumas, Marc; Thoenen, Hans. Department of Neurology, University of Maryland School of Medicine, Baltimore, MD 21201 **Retrograde axonal transport of nerve growth factor in the ciliary ganglion of the chick and the rat.** Brain Research (Amsterdam). 159(2):411-415, 1978.

Retrograde axonal transport of nerve growth factor (NGF) in parasympathetic neurons was examined by injecting 125-I labeled NGF unilaterally into the anterior eye chamber of rats and intraocularly in chicks. The preferential accumulation of radioactivity in the ciliary ganglion on the injected side was taken as an index of retrograde axonal transport from the nerve terminals supplying the iris. NGF was taken up and transported by parasympathetic neurons of both the chick and rat ciliary ganglion. In the chick ciliary ganglia, only a limited population of neurons projecting to the iris seemed to possess this transport capability, whereas all the projecting neurons in the rat seemed to bind, take up, and transport NGF. No accumulation of NGF in the submandibular ganglion was observed, indicating that retrograde axonal transport of NGF is not a common property of all peripheral parasympathetic neurons. 16 references.

003006 McLennan, H.; Hicks, T. P. Department of Physiology, University of British Columbia, 2075 Wesbrook Place, Vancouver, British Columbia, V6T 1W5, Canada **Pharmacological characterization of the excitatory cholinergic receptors of rat central neurones.** Neuropharmacology (Oxford). 17(6):329-334, 1978.

The actions of acetylcholine (ACh) and of various cholinomimetics on neurones in the rat central nervous system were determined. Excitations of cortical and ventrobasal thalamic neurones and of Renshaw cells of the spinal cord in response to ACh were mimicked both by muscarinic and nicotinic agonists. The excitations elicited by ACh and acetyl-beta-methylcholine were antagonized by atropine, and those produced by ACh and nicotinic agonists were blocked by dihydro-beta-erythroidine, curare, and mecamylamine. Excitatory ACh receptors in the rat appear to differ from those in the cat and cannot be easily described as muscarinic, nicotinic, or mixed; the receptors appear to lack selectivity toward the pharmacological agents with which they interact. 26 references. (Author abstract modified)

003007 McMillen, Brian A.; Isaac, Lawrence. Department of Pharmacology, University of Illinois at the Medical Center, Chicago, IL 60680 **Effects of pentylenetetrazol and trimethadione on**

feline brain monoamine metabolism. Biochemical Pharmacology (Oxford). 27(14):1815-1820, 1978.

The effects of pentylenetetrazol (PTZ) on behavioral excitation and brain monoamine metabolism were investigated in cats by monitoring the EEG and assaying the cerebrospinal fluid (CSF) for monoamine metabolites. After a nonconvulsant dose of PTZ, neither the concentrations of the 5-hydroxytryptamine (5-HT) metabolite, 5-hydroxyindoleacetic acid (5-HIAA), nor the dopamine (DA) metabolite, homovanillic acid (HVA), were altered in CSF if the rectal temperature of the cat was maintained. After a convulsant dose, there was an increase in 5-HIAA and HVA levels. The norepinephrine (NE) metabolite, 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG), was also increased, but returned to control values within 3 hours, whereas 5-HIAA and HVA levels were elevated for 24 hours. Trimethadione produced a transient decrease in HVA levels. When convulsions, but not EEG excitation, were prevented by trimethadione pretreatment, brain monoamine metabolism was increased. Plasma tryptophan levels decreased after convulsant doses of PTZ. PTZ was not detectable in plasma or in CSF 24 hours after injection, while CSF 5-HIAA and HVA levels were still increased. Results indicate that PTZ directly increases brain, NE, DA and 5-HT metabolism while causing EEG excitatory changes. 36 references. (Author abstract)

003008 Means, Jeffrey R.; Schnell, R. Craig; Miya, Tom S.; Bousquet, William F. Dept. of Pharmacology and Toxicology, School of Pharmacy and Sciences, Purdue University, West Lafayette, IN 47907 **Correlation of phenobarbital- and SKF 525-A-induced modification of pentobarbital hypnosis with alteration of in vivo and in vitro pentobarbital metabolism in the rat.** Pharmacology (Basel). 16(4):181-192, 1978.

The ability of various in vitro and in vivo pentobarbital metabolizing systems to reflect modifications in pentobarbital response following treatment with either phenobarbital or SKF 525-A was assessed in Sprague-Dawley rats. Of the in vitro systems studied, the hepatic 10,000g supernatant and washed microsome fractions and liver slices reflected varying degrees of phenobarbital-induced stimulation of pentobarbital metabolism. Significant SKF-525-A induced inhibition of pentobarbital metabolism, in the hepatic microsome fraction, liver slices, and isolated perfused liver were observed. Plasma level decline of pentobarbital, however, was identified as the measure of pentobarbital metabolism which best reflects both phenobarbital- and SKF-525A-induced modification of the duration of pentobarbital response. In correlating the in vitro systems with the in vivo systems of pentobarbital metabolism, both the hepatic microsome fractions reflected phenobarbital-induced alteration of in vivo pentobarbital metabolism as determined by plasma level decline, while none of the in vitro metabolism systems employed adequately reflected modification of the in vivo metabolism of the barbiturate following SKF 525-A treatment. The existence of major differences in the sensitivity and responsiveness of in vitro hepatic and in vivo systems in their capacity to reflect modification of pentobarbital response and metabolism following phenobarbital and SKF 525-A treatment are indicated. 31 references. (Author abstract modified)

003009 Meltzer, H. Y.; Simonovic, M.; Fang, V.; Piyakalamala, S.; Young, M. Department of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago, IL **A comparison of the effects of anti-psychotic drugs on pituitary, striatal and limbic system post-synaptic dopamine receptors.** Life Sciences (Oxford). 23(6):605-609, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Atagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the effects of antipsychotic drugs on pituitary, striatal, and limbic system postsynaptic dopamine (DA) receptors are reported. Clozapine, 2-chloro-11-3dimethylaminopropylidene morphanthridine trebenzomine, and sultopride had much weaker effects on human and rat prolactin (PRL) secretion than would be expected on the basis of their antipsychotic potency. The reverse was true of two other benzamides, sulpiride and metoclopramide. Classical neuroleptics of the phenothiazine, butyrophenone, and thioxanthene types affected rat and human PRL secretion in a manner that was mainly but not entirely consistent with their known effects on striatal and mesolimbic/mesocortical postsynaptic DA receptors. Preliminary studies indicate that presynaptic receptors that affect prolactin secretion are not present in rats. Supersensitivity may develop in the tuberoinfundibular system after chronic neuroleptic treatment but altered sensitivity of these receptors was not found in schizophrenics given apomorphine. 26 references. (Author abstract modified)

003010 Meltzer, Leonard T.; Moreton, J. Edward; Khazan, Naim. Department of Pharmacology and Toxicology, University of Maryland School of Pharmacy, Baltimore, MD 21201 **Electroencephalographic and behavioral tolerance and cross-tolerance to morphine and methadone in the rat.** Toxicology and Applied Pharmacology. 45(3):837-844, 1978.

Electroencephalographic (EEG) and electromyographic activity were recorded continuously in female Sprague-Dawley rats made tolerant by chronic intravenous administration of morphine (10mg/kg/2 hours) or methadone (2mg/kg/1.5hours). The effects on the EEG and gross behavior of intravenous challenge doses of morphine (10, 20, and 40mg/kg) and methadone (1, 2, and 4mg/kg) in naive and tolerant rats were also assessed. In naive rats, 2 and 4mg/kg methadone were equipotent with 10 and 20mg/kg morphine in regard to the duration of induced EEG slow burst activity and behavioral stupor, but methadone was about 10 times as effective as morphine in increasing the EEG voltage. Tolerance to these effects developed more quickly to morphine than to methadone. Methadone tolerant rats showed a high degree of cross-tolerance to morphine, but morphine tolerant rats showed very low cross-tolerance to methadone. It is concluded that results of this study may shed reported high incidence of methadone related toxicities among heroin dependent individuals. 22 references. (Author abstract modified)

003011 Mercer, L. F., Jr.; Remley, N. R.; Gilman, D. P. University of Texas Health Science Center, San Antonio, TX 78284 **Effects of urethane on hippocampal unit activity in the rat.** Brain Research Bulletin. 3(5):567-570, 1978.

The effect of urethrane on hippocampal single unit activity in male Sprague-Dawley rats paralyzed with gallamine triethiodide was examined to determine possible influences of urethane as an anesthetic for electrophysiological recordings. With intravenous injections of 1.0g/kg urethane, hippocampal units responded initially with a substantial decrease in spontaneous firing rate. Activity in some cells recovered partially after about 45 minutes. The activity of the rest of the cells remained depressed about 1.5hours; longer periods of depression were observed in some cells. Results demonstrate differences in time course of suppression of hippocampal unit activity which may be involved in changes in hippocampal theta activity under urethane. 10 references. (Author abstract modified)

003012 Messing, Rita B.; Flinchbaugh, C.; Waymire, J. C. Department of Psychobiology, University of California at Irvine, Irvine, CA 92717 **Changes in brain tryptophan and tyrosine following acute and chronic morphine administration.** Neuropharmacology (Oxford). 17(6):391-396, 1978.

Morphine increased brain concentrations of tryptophan and tyrosine 1 to 2 hours after administration in a dose dependent manner in male rats. Concentrations of these amino acids in blood serum decreased 30 to 45 minutes after injection and then rose toward control values. The rise in brain amino acids was antagonized by pretreatment with naloxone. In addicted rats, there was only a slight increase in brain tryptophan and no increase in tyrosine. Thirty minutes after naloxone precipitated withdrawal, tryptophan and tyrosine concentrations were elevated in brain, in contrast to the decline in these amino acids seen after naloxone administration in acutely morphinized rats. Findings support the hypothesis that the elevated turnover of brain monoamines induced by morphine is related to increased availability of precursor amino acids in morphinized animals. 40 references. (Author abstract)

003013 Meza-Ruiz, Graciela; Tapia, Ricardo. Instituto de Biologia, Universidad Nacional Autonoma de Mexico, Apartado Postal 70-600, Mexico 20, D.F., Mexico **(3H)GABA release in synaptosomal fractions after intracranial administration of ruthenium red.** Brain Research (Amsterdam). 154(1):163-166, 1978.

Glutamate decarboxylase (GAD) activity in brain homogenates and (3H)gamma-aminobutyric acid (GABA) uptake and release were examined in mice following intracranial injection of ruthenium red. In synaptosomes from ruthenium red treated animals, the Ca2 stimulated release of GABA was reduced to 64.5% of that in control mice. Neither (3H)GABA uptake by synaptosomal fractions nor GAD activity in brain homogenates was significantly modified. Results suggest that ruthenium red produces convulsion by blocking the Ca2 dependent release of GABA from inhibitory nerve endings. 24 references.

003014 Micic, D.; Klatzo, I.; Spatz, M. Section on Neurocytobiology, Laboratory of Neuropathology and Neuroanatomical Sciences, NINCDS, NIH, Bethesda, MD 20014 **The effect of sodium pentobarbital on some mitochondrial enzymes.** Journal of Neurochemistry (Oxford). 30(6):1627-1628, 1978.

A transient pentobarbital inhibition of monoamine oxidase (MAO) and cytochrome oxidase (CyO) activities which was observed during the investigation of ischemic effect on some mitochondrial enzymes, is described. Mongolian gerbils in groups of 12 animals were anesthetized with intraperitoneal injection of Na pentobarbital and killed by decapitation after 90 to 270 minutes or after 24 hours. Progressively decreased activities of both MAO and CyO were observed up to 150 min. posttreatment. MAO was affected more significantly than CyO activity at 90 min, but MAE recovery occurred earlier than that of CyO activity. Results are suggestive of barbiturate interference with oxygen uptake. Pentobarbital and other anesthetics may conceivably affect the level of neurotransmitters in the brain. 13 references.

003015 Mickel, Robert A.; Hallidy, Leslie; Haugaard, Niels; Haugaard, Ella S. Department of Pharmacology, University of Pennsylvania, School of Medicine, Philadelphia, PA 19104 **Stimulation by lithium ions of the incorporation of (U-14C)glucose into glycogen in rat brain slices.** Biochemical Pharmacology (Oxford). 27(5):799-800, 1978.

The effect of lithium ions on the incorporation of glucose into glycogen in male Wistar rat brain slices was determined. Addition of 25mM lithium chloride (LiCl) to the incubation medium resulted in statistically significant stimulation of the incorporation of (U-14C)glucose into glycogen at all times greater than 10 minutes. In a second experiment, brain slices were incubated for one hour with (U-14C)glucose. As the concentration of LiCl in the medium was raised, there was a progressive increase in the incorporation of isotope into glycogen. A significant effect of lithium was obtained at concentrations as low as 0.5mM and the maximum effect of the lithium ion was observed at about 5mM. Result 5 indicate that lithium ions have a direct stimulatory effect on the rate of glycogen synthesis from glucose in brain. The effect of lithium on glycogen metabolism occurs at concentrations similar to those estimated to exist in brain tissue of patients undergoing therapy with lithium salts. 16 references.

003016 Miller, Harold H.; Clarke, David E. Department of Pharmacology, College of Pharmacy, University of Houston, Houston, TX 77004 **In vitro inhibition of monoamine oxidase types A and B by d- and l-amphetamine.** Communications in Psychopharmacology. 2(4):319-326, 1978.

The monoamine oxidase (MAO) inhibitory properties of d-amphetamine and l-amphetamine were investigated in vitro in various Wistar rat tissues. The MAO inhibitory potency of d-amphetamine was greatest in tissues showing high type. A activity (heart, striatum and vas deferens, liver, in descending order). The two enantiomers were equally potent in inhibiting type B activity. Both enantiomers were more potent inhibitors of type MAO than of type B. On type A MAO, d-amphetamine was more than four times as potent as i-amphetamine in all tissues studied. The data suggest that inhibition of type A MAO by d-amphetamine is an important pharmacological property of the drug in vivo. The individual characteristics of the A and B activities do not appear to differ radically across the various tissues studied. 11 references. (Author abstract modified).

003017 Mishra, Radhakanta; Sulser, Fridolin. Vanderbilt University School of Medicine, Nashville, TN 37232 **Role of serotonin reuptake inhibition in the development of subsensitivity of the norepinephrine (NE) receptor coupled adenylate cyclase system.** Communications in Psychopharmacology. 2(4):365-369, 1978.

The effects of antidepressant drugs that alter the availability of serotonin (5-hydroxytryptamine, 5-HT) on the norepinephrine (NE) receptor coupled adenylate cyclase system were investigated in male Sprague-Dawley rats. Basal levels of cyclic adenosine monophosphate (AMP) in the limbic forebrain and sensitivity to NE were not altered by the 5-HT uptake inhibitors chlorimipramine and fluoxetine or by amitriptyline. However, within 2 weeks, chlorimipramine and amitriptyline reduced the neurohormonal response to NE, while fluoxetine did not alter the sensitivity. It is concluded that a change in the availability of 5-HT per se does not change the sensitivity of the cyclic AMP generating system to NE and that the effects of chlorimipramine and amitriptyline may be due to the in vivo conversion to their secondary amines, which are potent inhibitors of the neuronal uptake of NE. 19 references. (Author abstract modified)

003018 Mishra, Ram K. Neuropharmacology Laboratory, Department of Psychiatry, McMaster University Medical Centre, Hamilton, Ontario, Canada **Effect of substituted benzamide drugs on rat striatal tyrosine hydroxylase.** European Journal of Pharmacology (Amsterdam). 51(2):189-190, 1978.

To assess the presynaptic action of sulpiride and other benzamides on the dopaminergic system, the effects of the drugs on tyrosine hydroxylase activity in rat striatal tissue were investigated. Apomorphine caused significant inhibition of tyrosine hydroxylase activity in synaptosomal preparations. This inhibitory effect was reversed by haloperidol, sulpiride, metoclopramide, clebopride, and tigan. Results suggest that sulpiride and other centrally active benzamide derivatives achieve their effect primarily by interacting with presynaptic dopaminergic mechanisms. However, their interaction with postsynaptic dopamine

receptors other than those coupled with adenylate cyclase could not be ruled out. 4 references.

003019 Misra, A. L.; Vadlamani, N. L.; Pontani, R. B. New York State Office of Drug Abuse Services Research Laboratory, 80 Hanson Place, Brooklyn, NY 11217 **Clearance and analgesic activity of the quaternized opiate, N-methylmorphine (6-3H) administered intracisternally to the rat.** Journal of Pharmacy and Pharmacology (London). 30(3):187-188, 1978.

The preparation, clearance, and analgesic activity of the quaternized opiate N-methylmorphine (6-3H) were examined in male Wistar rats. The comparative analgesic activities of morphine and N-methylmorphine (0.5mg/kg, intracisternally) were determined by measuring the mean latencies of pain responses in rats placed on a hotplate. The quaternary compound had substantially lower analgesic potency and a shorter duration of action compared to morphine, and it produced morphine-like sedation after a brief period of initial excitation. The time course of efflux of N-methylmorphine from the central nervous system into plasma correlated with its pharmacological activity. Chromatography of pooled plasma samples did not reveal any biotransformation of N-methylmorphine to morphine, indicating that the analgesia observed was due to the quaternary compound itself and not to in vivo conversion to the tertiary amine. 8 references.

003020 Mitra, Chhanda; Guha, S. R. Indian Institute of Experimental Medicine, Calcutta, India **Inhibition of monoamine oxidation in subfractions of crude mitochondria of rat brain by clorgyline and Lilly 51641.** Biochemical Pharmacology (Oxford). 27(20):2455-2457, 1978.

The inhibition of monoamine oxidase (MAO) activity by clorgyline and chlorphenoxy ethyl cyclopropylamine (Lilly 51641) was studied in crude mitochondria of rat brain, using tyramine and serotonin as substrates. Results indicate that type A and type B MAO are distributed in different ratios among mitochondrial subfractions. Fraction C was predominantly made up of type A MAO and fraction D constained a fairly even mixture of both types. Fraction E contained predominantly type B MAO, with only slight contamination of type A MAO. 16 references.

003021 Moleman, Peter; Bruinvels, Jacques; van Valkenburg, Cornelius F. M. Department of Psychiatry, Academic Hospital Dijkzigt, Dr. Molewaterplein 40, Rotterdam, Netherlands **On the relation between haloperidol-induced alterations in DA release and DA metabolism in rat striatum.** Life Sciences (Oxford). 23(6):611-615, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the effects of haloperidol (1mg/kg) on dopamine (DA), homovanillic acid (HVA), and 3,4-dihydroxyphenylacetic acid (DOPAC) levels in the striatum of male Wistar rats pretreated with aplha-methyl-para-tyrosine (aMPT) are reported. Haloperidol stimulated DA release for at least 60 minutes, while HVA and DOPAC levels were markedly increased only at 30 minutes after drug administration. In rats not pretreated with aMPG, however, a strong increase in metabolite levels was observed between 60 and 120 minutes after haloperidol. DA biosynthesis and processes involved with the clearance of metabolites appear to be important factors in the haloperidol-induced increases in metabolite levels, but no evidence for a direct relationship between DA release and metabolite levels was obtained. 7 references. (Author abstract modified)

003022 Monti, Jaime M.; Altier, Humberto; Ziman, Vilma. Departamento de Farmacologia y Terapeutica, Hospital de Clinicas, Pl Montevideo, Uruguay **The effects of p-chlorophenylalanine, reserpine, methysergide and cyproheptadine on the dopa-induced EEG synchronization in the rat.** European Journal of Pharmacology (Amsterdam). 50(3):183-186, 1978.

The actions of drugs that interfere with central indolaminergic mechanisms were assessed on the DOPA-induced EEG synchronization in male Wistar rats. The increased slow wave activity observed during the first 30 minutes following 100mg/kg DOPA was significantly decreased by 400mg/kg p-chlorophenylalanine, 4 and 8mg/kg reserpine, and 16mg/kg methysergide. Cyproheptadine was ineffective in this respect. The findings lend support to the hypothesis that the initial synchronization after DOPA is related to the release of 5-hydroxytryptamine. 11 references. (Author abstract)

003023 Moss, D. E.; Peck, P. L.; Salome, R. Department of Psychology, University of Texas at El Paso, El Paso, TX 79968 **Tetrahydrocannabinol and acetylcholinesterase.** Pharmacology Biochemistry and Behavior. 8(6):763-765, 1978.

To determine whether the psychoactive effects of delta9-tetrahydrocannabinol (delta9-THC), are related to cholinergic activity, the interaction between acetylcholinesterase (AChE) and delta9-THC was studied in a sample of 20 rats. Results indicate there is no physiologically important interaction between AChE and delta9THC or its metabolites that could explain its psychoactive effects or the clinical depression observed when human marihuana users are administered the cholinesterase inhibitor, physostigmine. 24 references. (Author abstract modified)

003024 Muller, Walter E.; Snyder, Solomon H. Pharmakologisches Institut der Universitat Mainz, Obere Zahlbacher Strasse 67, D-65 Mainz, Germany **Strychnine binding associated with synaptic glycine receptors in rat spinal cord membranes: ionic influences.** Brain Research (Amsterdam). 147(1):107-116, 1978.

Ionic influences on strychnine binding in spinal cord membranes were examined in male Sprague-Dawley rats. Ammonium salts of some anions decreased the potency of glycine in inhibiting (3H)strychnine binding associated with synaptic glycine receptors. The ability of the ammonium salts of anions to increase the concentration of glycine, required to inhibit specific (3H)strychnine binding, corresponded to their capacity to reduce the (3H)strychnine binding itself and their capacity to reverse inhibitory postsynaptic potentials. The decrease of (3H)strychnine binding in the presence of chloride was abolished by sodium, while the decrease of the potency of glycine in inhibiting (3H)strychnine was not. Binding of (3H)strychnine was influenced by monovalent cations in a biphasic fashion; concentrations of lithium, potassium, and sodium cations up to 150mM decreased (3H)strychnine binding, while higher concentrations of the cations increased (3H)strychnine binding. Inhibition by glycine of (3H)strychnine binding was enhanced by low concentrations of these cations. 16 references. (Author abstract modified)

003025 Muskeit, Frits A. J.; Jeuring, Hans J.; Ader, J.-P.; Wolthers, Bert G. Central Laboratory, University Hospital, Oostersingel 59, Groningen, The Netherlands **Identification and quantification of 3-methoxy-4-hydroxyphenylethanol (MOPET) in human cerebrospinal fluid and rat brain by means of gas chromatography -- mass spectrometry.** Journal of Neurochemistry (Oxford). 30(6):1495-1499, 1978.

The identification of 3-methoxy-4-hydroxyphenylethanol (MOPET) in human cerebrospinal fluid and in rat brain is described. Use was made of the high sensitivity and selectivity provided by gas chromatography mass spectrometry. Concentrations of MOPET in human cerebrospinal fluid, rat brain, and rat urine together with those of some other catecholamine metabolites are given. The effect of intraperitoneal administration of deuterium labelled MOPET and haloperidol on rat brain and

urine MOPET levels was studied. The quantitative importance of MOPET as an end product of central and peripheral dopamine metabolism in man and rat is discussed. 13 references. (Author abstract)

003026 Myers, Paul R.; Blosser, James; Shain, William. Central Research and Development Department, E. I. du Pont de Nemours & Co., Experimental Station, Wilmington, DE 19898 **Neurotransmitter modulation of prostaglandin E1-stimulated increases in cyclic AMP. II. Characterization of a cultured neuronal cell line treated with dibutyryl cyclic AMP.** Biochemical Pharmacology (Oxford). 27(8):1173-1177, 1978.

The ability of selected neurotransmitters to modulate prostaglandin E1 (PGE1) stimulated increases in cyclic adenosine monophosphate (AMP) was tested in the somatic cell hybrids TCX 17 and TCX 11 differentiated by growth in dibutyryl cyclic AMP. PGE1 caused an increase in cellular cyclic AMP. Carbachol, noradrenaline (NA), and dopamine (DA) inhibited the effect of PGE1, while 5-hydroxytryptamine had no effect. The carbachol inhibition was reversed by scopolamine and unaffected by nicotinic antagonists, indicating that the inhibition was mediated by a muscarinic receptor. The NA inhibition was reversed by phenoxybenzamine and phentolamine, but not by the beta-antagonists propranolol and dichloroisoproterenol. The DA inhibition was reversed by chlorpromazine and trifluoperazine. The DA agonist ET495 mimicked DA, while apomorphine had little or no effect. These biochemical results obtained from differentiated cells are compared to those reported for exponential growth phase cells of the same cell line and with electrophysiological results reported for the cell lines. 14 references. (Author abstract modified)

003027 Nakahara, T.; Uchimura, H.; Saito, M.; Hirano, M.; Kim, J. S.; Ito, M. Department of Chemistry, Faculty of Science, Kyushu University, Hakozaki, Fukuoka 812, Japan **Inhibition of dopamine-sensitive adenylate cyclase in rat striatum by neuroleptic drugs administered in vivo.** Journal of Neurochemistry (Oxford). 31(5):1335-1337, 1978.

The effects of chlorpromazine (CPZ) and haloperidol (HAL) on the dopamine (DA) sensitive adenylate cyclase in male Wistar-King rat striatal homogenates were investigated after in vitro or in vivo drug administration. The DA stimulated adenylate cyclase activity in rat striatal homogenates was competitively inhibited by CPZ and HAL added in vitro; the inhibitory constant values for CPZ and HAL were 0.13 and 0.052microM, respectively. Intraperitoneal injection of CPZ and HAL increased the DA concentration required for half maximal stimulation (apparent Km) of adenylate cylase activity in striatal homogenates. A slight decrease in DA stimulated activity and a significant decrease in apparent Km for DA occurred 2 hours after intraperitoneal injection of HAL. The neuroleptic drug and its active metabolites that accumulated in striatum after acute treatment with the drug caused a detectable inhibitory effect on adenylate cyclase activity measured in vitro. CPZ (90mg/kg) and haloperidol (10mg/kg) produced a similar increase in the apparent Km, indicating that HAL is nine times more potent than CPZ in reducing DA adenylate cyclase response when the drugs are given in vivo. 11 references.

003028 Neill, Darryl B.; Peay, Lynn A.; Gold, Marc S. Department of Psychology, Emory University, Atlanta, GA 30322 **Identification of a subregion within rat neostriatum for the dopaminergic modulation of lateral hypothalamic self-stimulation.** Brain Research. 153(3):515-528, 1978.

Experiments were conducted to test the hypothesis that the involvement of neostriatal dopaminergic transmission in lateral hypothalamic self-stimulation might be specific to a striatal subregion. Crystalline application of dopamine (DA) or d-amphetamine increased self-stimulation rates only when made to ventral anterior striatum (VAS); more dorsal or posterior applications were ineffective. A comparison of dose response functions for DA using solution injections in VAS and posterior striatum (PS) confirmed that only VAS was responsive. Injections or applications of 6-hydroxydopamine suppressed responding only when made into VAS. Haloperidol injections decreased responding only for VAS and not PS injection sites. Applications or injections of scopolamine often increased responding when made into VAS, but this effect was unreliable. Applications or injections of scopolamine to more posterior sites consistently suppressed responding. It was concluded that dopaminergic transmission in VAS, alone among the striatal sites tested, is facilitatory on hypothalamic self-stimulation. The effects of drug applications to nucleus accumbens were generally similar to VAS, and it was suggested that these areas may be functionally similar. Examination of the known afferents to VAS indicated that this area may be influenced by activity in limbic structures. This anatomy may help provide an understanding of how neostriatum might be involved in central reward processes. 45 references. (Author abstract)

003029 Nelson-Krause, Diana C.; Howard, Bruce D. Division of Neurosciences, City of Hope National Medical Center, Duarte, CA 91010 **Energy utilization in the induced release of gamma-aminobutyric acid from synaptosomes.** Brain Research (Amsterdam). 147(1):91-105, 1978.

Newly accumulated gamma-aminobutyric acid (GABA) was released from synaptosomes by treatment with 30mM potassium ion (K) or the calcium ion (Ca2) inophore A23187. Release was Ca2 dependent and energy dependent. The induced release of GABA was inhibited by S-13 (5-chloro-3-t-butyl-2'-chloro-4-nitrosalicylanilide), an uncoupler of oxidative phosphorylation; by azide, a blocker of mitochondrial respiration; and by oligomycin, efrapeptin, tributyltin, and dicyclohexylcarbodiimide, which are inhibitors of Ca2/Mg2 adenosine triphosphatases. Efrapeptin blocked GABA release induced by K but not by A23187-induced release. Azide and oligomycin appeared to inhibit GABA release as a consequence of their effects on mitochondrial adenosine triphosphate (ATP) synthesis. Inhibition of GABA release by the other compounds could not be totally accounted for by their effects on synaptosomal ATP stores. It is suggested that these compounds, in addition to affecting ATP synthesis, directly affect biochemical reactions involved in GABA release. 46 references. (Author abstract modified)

003030 Nielsen, Erik B.; Lyon, Melvin. Psychopharmacological Research Laboratory, Sct. Hans Mental Hospital, DK-4000 Roskilde, Denmark **Evidence for cell loss in corpus striatum after long-term treatment with a neuroleptic drug (flupenthixol) in rats.** Psychopharmacology (Berlin). 59(1):85-89, 1978.

The number of nerve cells in the ventrolateral and dorsomedial areas of the corpus striatum was estimated in male Wistar rats treated for 36 weeks with weekly intramuscular injections of the neuroleptic flupenthixol (4mg/kg). Fourteen to 18 weeks after the last drug injection, the animals were decapitated; half of each brain was fixated with formalin for cell count analysis and half was used for biochemical analysis. Separate cell counts in the ventrolateral and dorsomedial corpus striatum yielded a cell loss of approximately 10% in the ventrolateral striatum. Results indicate that persistent irreversible anatomical changes can occur following long-term neuroleptic treatment. 27 references. (Author abstract modified)

003031 Norberg, Karin; Scatton, Bernard; Korf, Jakob. Synthelabo, Department of Biology, Cerebral Circulation and Metabolism Unit, Neurochemistry Unit, F-92220 Bagneux, France **Am-**

phetamine-induced increase in rat cerebral blood flow; apparent lack of catecholamine involvement. Brain Research (Amsterdam). 149(1):165-174, 1978.

The influence of intraperitoneal administration of 5mg/kg D,L-amphetamine on regional cerebral blood flow (CBF) in male rats was examined after surgically or pharmacologically-induced depletion of brain catecholamines. Bilateral removal of the superior cervical ganglion did not prevent the amphetamine-induced augmentation of CBF; maximal changes occurred in the frontal and parietal cortex. Destruction of the ascending noradrenergic pathways by unilateral or bilateral injections of 6-hydroxydopamine, which decreased the noradrenaline (NA) level in the frontal cortex by 89%, was ineffective in abolishing the increase in CBF caused by amphetamine in the frontal cortex. The involvement of other catecholaminergic systems was excluded by pretreatment of the rats with reserpine plus alpha-methyl-p-tyrosine, which reduced the levels of NA, dopamine, and adrenaline in the frontal cortex by 92%, 97%, and 99%, respectively; this treatment did not alter the effect of amphetamine on CBF in the frontal cortex. Results suggest that the action of amphetamine on CBF is not mediated mainly by catecholamines. 24 references. (Author abstract modified)

003032 O'Dea, Robert F.; Gagnon, Claude; Zatz, Martin. Division of Clinical Pharmacology, University of Minnesota Medical School, 10 5 Millard Hall, Minneapolis, MN 55455 **Regulation of guanosine 3',5'cyclic monophosphate in the rat pineal and posterior pituitary glands.** Journal of Neurochemistry (Oxford). 31(3):733-738, 1978.

Potassium (K) and norepinephrine (NE) stimulated the accumulation and efflux of cyclic adenosine monophosphate (AMP) and cyclic guanosine monophosphate (GMP) in Sprague-Dawley rat pineal glands. The efflux of both cyclic nucleotides was blocked by probenecid. The accumulation and efflux of cyclic GMP, but not of cyclic AMP, depended on the presence of intact nerve endings and extracellular calcium (Ca2). The Ca2 dependent release of NE caused by veratridine was accompanied by the efflux of both cyclic nucleotides. In contrast, the Ca2 independent release of NE caused by tyramine was accompanied by the efflux of cyclic AMP but not of cyclic GMP. High concentrations of K, also increased tissue levels of cyclic GMP in the posterior pituitary gland. Veratridine and K, but not NE, stimulated the efflux of cyclic GMP from this neurosecretory gland. The enhanced accumulation of cyclic GMP in the pineal gland after K did not appear to be mediated by extracellular NE. Desmethylimipramine blocked the NE stimulated changes in cyclic GMP, but not those caused by K. Seasonal variations in the response of pineal cyclic GMP to K and NE are also discussed. 30 references. (AUthor abstract modified)

003033 Oakley, N. R.; Dray, A. Department of Pharmacology, School of Pharmacy, University of London, London WC1N 1AX, England **The effects of ethanolamine-O-sulphate injection into the rat substantia nigra: electrophysiological studies.** Brain Research (Amsterdam). 153(2):387-391, 1978.

The effects of injection of the irreversible gamma-aminobutyric acid (GABA) transaminase inhibitor, ethanolamine-O-sulphate (EOS), into the substantia nigra were examined electrophysiologically in male albino rats. Spontaneous activity in the substantia nigra zona reticulate was unchanged following EOS injection, but neurons in this region were less responsive to striatal stimulation. EOS significantly prolonged the latency of excitation evoked by striatal stimulation. In the striatum, neuronal firing was unchanged but nigrostriatal dopamine cell activity was increased. Results are discussed in terms of the functional relationship of the dopaminergic nigrostriatal pathway and striatonigral GABA fibers. 23 references.

003034 Oleson, Terrence D.; Twombly, Dennis A.; Liebeskind, John C. Dept. of Psychology, University of California, Los Angeles, CA 90024 **Effects of pain-attenuating brain stimulation and morphine on electrical activity in the raphe nuclei of the awake rat.** Pain (Amsterdam). 4(3):211-230, 1978.

To shed further light on the role of the raphe nuclei in neural mechanisms of antinociception, the effects of analgesic brain stimulation and morphine on spontaneous and evoked activity were examined and compared in the dorsal raphe, median raphe, and raphe magnus of rats. Evoked potential and multiple unit responses to noxious shock and pinch as well as to innocuous air puffs were recorded, and concurrent measurements of various behavioral responses to noxious stimuli were also made. Electrical stimulation of midbrain central gray and of medial thalamus, as well as systemic administration of morphine, greatly diminished all behavioral and electrophysiological responses to noxious stimuli without reliably affecting responses to air puffs. At the same time that brain stimulation and morphine attenuated nociceptive responses, a significant elevation was seen in the spontaneous multiple unit activity of these brain areas, particularly nucleus raphe magnus. In another group of animals, a comparison was made of the analgesic effectiveness of stimulation sites in the bulbar raphe (including raphe magnus) and sites dorsal or lateral to this region. More consistently potent effects were obtained from the raphe placements. These findings point to the importance of the bulbar raphe in mechanisms of analgesia. It is suggested that brainstem stimulation and morphine administration activate descending controls of raphe origin which selectively inhibit nociceptive elements in the spinal cord. 34 references. (Author abstract)

003035 Page, Ellen D.; Neufeld, Arthur H. Department of Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, CT 06510 **Characterization of alpha-adrenergic and beta-adrenergic receptors in membranes prepared from the rabbit iris before and after development of supersensitivity.** Biochemical Pharmacology (Oxford). 27(6):953-958, 1978.

Alpha-adrenergic and beta-adrenergic receptors were studied by measuring the binding of (3H)dihydroergocryptine (DHEC) and (3H)dihydroalprenolol (DHAP), respectively, to membranes prepared from homogenized New Zealand rabbit iris. The binding of DHEC appeared to be specific for alpha-adrenergic receptors, as adrenergic agents displaced this radioligand with the following order of potency: phentolamine, epinephrine, norepinephrine, isoproterenol and propranolol. The binding of DHAP appeared to be specific to beta-adrenergic receptors, as adrenergic agents displaced this radioligand with the following order of potency: propranolol, isoproterenol, epinephrine, norepinephrine, phentolamine. Several weeks after removal of the superior cervical ganglion, when all the adrenergic nerves to the tissue had degenerated, membranes prepared from denervated iris had an increased density of beta-adrenergic receptors with no increase in the density of alpha-adrenergic receptors. The affinities of the receptors did not change. Results suggest that unlike skeletal muscle, the supersensitivity that occurs in smooth muscle is not due to an increase in the population of receptors governing contraction. The change in population of beta-adrenergic receptors, however, is consistent with the hypothesis that the level of cyclic adenosine monophosphate modulates the density of the beta-adrenergic receptor. 30 references. (Author abstract modified)

003036 Palacios, Jose-Maria; Schwartz, Jean-Charles; Garbarg, Monique. Unite 109 de Neurobiologie, Centre Paul Broca de l'INSERM, 2ter, rue d'Alesia, F-75014 Paris, France **High affinity binding of 3H-histamine in rat brain.** European Journal of Pharmacology (Amsterdam). 50(4):443-444, 1978.

Tritiated histamine (HA) was used to reveal high affinity HA binding sites in rat brain. A single class of binding sites with a dissociaton constant value of 9.4nM was found in cerebral cortex. Marked differences in regional binding and selective inhibition by histaminergic agents suggest that these high affinity binding sites represent true HA receptors. The regional distribution of 3H-HA binding sites did not closely correlate with that of endogenous HA or 3H-mepyramine binding sites, but the highest binding occurred in regions containing histaminergic nerve terminals. The developmental pattern of high affinity 3H-HA binding sites in rat brain resembled that of L-histidine decarboxylase, a marker of histaminergic neurons. The selectivity of 3H-HA binding was supported by the lack of inhibition by various neurotransmitters, HA catabolites, and an HA methyltransferase inhibitor, S-adenosylhomocysteine. In contrast, the median inhibitory concentrations of a series of methyl derivatives of HA somewhat paralleled their activities as agonists. Results suggest that 3H-HA selectively labels HA receptors in brain, resembling typical H2-receptors. 4 references.

003037 Palfreyman, Michael G.; Huot, Sylvie; Lippert, Bruce; Schecter, Paul J. Centre de Recherche Merrell International 16, rue d'Ankara, F-67084 Strasbourg Cedex, France **The effect of gamma-acetylenic GABA, an enzyme-activated irreversible inhibitor of GABA-transaminase, on dopamine pathways of the extrapyramidal and limbic systems.** European Journal of Pharmacology (Amsterdam). 50(4):325-336, 1978.

Intraperitoneal injection of 100mg/kg of the gamma-aminobutyric acid (GABA) transaminase inhibitor, gamma-acetylenic GABA, (GAG), caused an increase in the concentration of GABA in male Sprague-Dawley rat brain. This increased GABA concentration was associated with a decreased rate of dopamine (DA) depletion following alpha-methyl-p-tyrosine treatment and a decrease in homovanillic acid in extrapyramidal and limbic structures, suggesting a decrease in DA turnover in both pathways. In addition, GAG injected into the ventral mesencephalic tegmentum decreased DA turnover in the mesolimbic forebrain. These results are consistent with a modulatory function of GABA containing neurons on extrapyramidal and limbic DA pathways. Inhibitory effects on DA functions of the extrapyramidal and limbic systems were also indicated by the amphetamine and apomorphine-induced ipsilateral turning after unilateral substantia nigral injections of GAG and by the attenuation of DA-induced hypermotility after bilateral injections of GAG into the nucleus accumbens. 34 references. (Author abstract modified)

003038 Palmer, Gene C.; Palmer, S. Jo. Department of Pharmacology, University of South Alabama College of Medicine, Mobile, AL 36608 **5'-Guanylyl-imidodiphosphate actions on adenylate cyclase in homogenates of rat cerebral cortex plus neuronal and capillary fractions.** Life Sciences. 23(3):207-215, 1978.

Norepinephrine (NE), isoproterenol (ISO), dopamine (DA), apomorphine (APO), histamine, 4-Me-histamine, and prostaglandins E1, E2, and A2 all activated adenylated cyclase in homogenates of rat frontal cortex. Adenylate cyclase in homogenates of isolated cortical neurons was sensitive to NE, ISO, DA, APO, histamine, 2-Me-histamine, and prostaglandin F2alpha. Capillary enriched fractions from the cortex possessed an enzyme that was activated by NE, ISO, and DA. Addition of 5'-guanylyl-imidodiphosphate, (Gpp(NH)p), to the cortical homogenates and neuronal fractions resulted in enhanced enzyme responses to NE, ISO, DA, 2-Me-histamine, 4-Me-histamine, and the prostaglandins E1 and E2. The actions of histamine and APO were not increased by the guanosine triphosphate analog. The sensititivy of the catecholamine-induced adenylate cyclase activation in cortical capillaries was augmented by Gpp(NH)p. Thus various cellular types within the cerebral cortex may possess different receptor characteristics with respect to stimulation of adenylate cyclase by neurohormones. 35 references. (Author abstract modified)

003039 Pappas, Bruce A.; Saari, Matti, Peters, David A. V.; Roberts, David C. S.; Fibiger, Hans C. Department of Psychology, Carleton University, Ottawa, Canada K1S 5B6 **Neonatal systemic 6-hydroxydopamine and dorsal tegmental bundle lesion: comparison of effects on CNS norepinephrine and the postdecapitation reflex.** Brain Research (Amsterdam). 155(1):205-208, 1978.

The effects of neonatal systemic 6-hydroxydopamine (NS-6-OHDA) and dorsal tegmental bundle (DTB) treatments on 13 discrete rat brain areas were compared. The postdecapitation reflex (PDR) was absent in the NS-6-OHDA rats, but neither its latency nor its duration were altered in the DTB rats. There were no effects of the two treatments on brain or spinal cord DA. Spinal norepinephrine (NE) was depleted by 48% in the NS-6-OHDA group but not affected in the DTB group. Forebrain, diencephalic, and brainstem NE depletion for the two groups were similar. The depletions of NE in cortex, hippocampus, olfactory area, anygdala, and hypothalamus were similar although more severe in the DTB rats. A striking difference was the total absence of NE in the septum of the DTB and the 39% depletion in the NS-6-OHDA. The reported observations point to a critical role of spinal NE in the postdecapitation reflex. 11 references.

003040 Parli, C. John; Schmidt, Barbara; Shaar, Carl J. Lilly Research Laboratories, Indianapolis, IN 46206 **Metabolism of lergotrile to 13-hydroxy lergotrile, a potent inhibitor of prolactin release in vitro.** Biochemical Pharmacology. 27(9):1405-1408, 1978.

The hydroxylated metabolite of lergotrile was identified as 13-hydroxy lergotrile. The effect of this metabolite on the release of prolactin in vitro was determined using a paired pituitary half incubation system and a double antibody radioimmunoassay. Results indicate that 13-hydroxy lergotrile is approximately 100 times more active than lergotrile in inhibiting the release of prolactin in vitro from the anterior pituitary. 13-Hydroxy lergotrile has been found to be a major metabolite in humans, but it is not known if it is active in vitro. 5 references.

003041 Pedigo, N. W.; Reisine, T. D.; Fields, J. Z.; Yamamura, H. I. Department of Pharmacology, University of Arizona Health Sciences Center, Tucson, AZ 85724 **3H-spiroperidol binding to two receptor sites in both the corpus striatum and frontal cortex of rat brain.** European Journal of Pharmacology (Amsterdam). 50(4):451-453, 1978.

The existence of two 3H-spiroperidol binding sites in both the frontal cortex and corpus striatum of male Sprague-Dawley rat brain was demonstrated. Scatchard analyses of saturation studies of 3H-spiroperidol binding over a wide range of ligand concentrations (1-4000pM) revealed two receptor sites with a 12-fold difference in affinity; the apparent dissociation constant values were 24-30pM for the high affinity site and about 340pM for the low affinity site. The corpus striatum contained primarily high affinity sites, while the low affinity sites predominated in the frontal cortex. Dopamine was a more potent inhibitor of 3H-spiroperidol binding in the corpus striatum than in the frontal cortex, but the reverse was true for serotonin. Several antipsychotic drugs also inhibited 3H-spiroperidol binding with different potencies in corpus striatum and frontal cortex; haloperidol and pimozide appeared to have a greater affinity for the type of receptor predominating in corpus striatum, while clozapine appeared to have greater affinity for the receptor predominating in the frontal cortex. These 3H-spiroperidol binding sites may represent dopaminergic and serotonergic receptors or may indicate

the presence of two classes of dopamine receptors, possibly presynaptic and postsynaptic. 5 references.

003042 Pericic, D.; Eng, N.; Walters, J. R. Rudjer Boskovic Institute, 41000 Zagreb, P.O.B. 1016, Yugoslavia **Post-mortem and aminooxyacetic acid-induced accumulation of GABA: effect of gamma-butyrolactone and picrotoxin.** Journal of Neurochemistry (Oxford). 30(4):767-773, 1978.

The effects of gamma-butyrolactone (GBL) and picrotoxin on both the postmortem and aminooxyacetic acid (AOAA)-induced accumulations of gamma-aminobutyric acid (GABA) were examined in rats. GBL produced a marked dose-dependent decrease in AOAA-induced GABA accumulation in caudate, globus pallidus, cerebellar and cerebral cortices. The cingulate cortex showed the greatest esponse to GBL; subanesthetic doses completely blocked the effect of AOAA. Picroxin increased the AOAA-induced accumulation of GABA in parietal, entorhinal, and cerebellar cortices and had no significant effect in pyriform and cingulate cortices. Neither drug significantly altered the postmortem accumulation of GABA. Results suggest that picrotoxin causes an increase in GABA synthesis in vivo. The apparent decrease in GABA synthesis following GBL treatment was greater than that observed with anesthetic doses of chloral hydrate and was not blocked by picrotoxin. Alterations in the activity of GABA neurons, cerebral glucose metabolism, and L-glutamate 1-carboxylase activity may contribute to the apparent decrease in in vivo GABA synthesis caused by GBL. 37 references. (Author abstract)

003043 Persson, Sven-Ake. Department of Pharmacology, University of Umea, S-901 87 Umea, Sweden **Effects of LSD and BOL on the catecholamine synthesis and turnover in various brain regions.** Psychopharmacology (Berlin). 59(2):113-116, 1978.

In male Sprague-Dawley rats lysergic acid diethylamide (LSD), 0.5mg/kg and 2-bromo lysergic acid diethylamide (BOL), 0.5mg/kg increased the rate of striatal tyrosine hydroxylation in vivo, as measured by the DOPA accumulation after decarboxylase inhibition. Neither LSD nor BOL significantly changed the DOPA accumulation in the olfactory tubercle, a dopamine (DA) rich part of the limbic system. LSD but not BOL increased the DOPA accumulation in the cerebral cortex and brainstem. LSD and BOL did not appear to alter the rate of alpha-methyl-p-tyrosine (AMPT)-induced disappearance of DA or of norepinephrine in the whole brain and did not change the rate of AMPT-induced disappearance of DA in the striatum. It is suggested that in the striatum, LSD and BOL block autoreceptors (presynatpic recptors) regulating the tyrosine hydroxylation; these receptors may be DA receptors or may be 5-hydroxytryptamine (5-HT) or LSD sensitive receptors. The regional differences observed between LSD and BOL suggest that LSD and BOL may differ in their effects on the 5-HT systems in the cerebral cortex and brainstem. 25 references. (Author abstract)

003044 Petkov, V. Institute of Physiology, Bulgarian Academy of Sciences, "Acad. G. Bonchev" Str., bl. 1, Sofia 1113, Bulgaria **Effect of ginseng on the brain biogenic monoamines and 3',5'-AMP system: experiments on rats.** Arzneimittel-Forschung (Aulendorf). 28(3):388-393, 1978.

The effects of ginseng on the content of biogenic monoamines in some brain structures, on the cyclic 3',5'-adenosine-monophosphate (AMP) system, and on the transport across the blood-brain barrier of the amino acid phenylalanine were investigated in male Wistar rats. Extract siccum ginseng pharmaton applied in an oral dose of 20mg/kg for 3 days improves the indices for learning and memory retention. Extract ginseng in a dose of 50mg/kg administered intraperitoneally for 5 days increased the dopamine and norepinephrine levels in the brainstem and decreased the serotonin level. In a dose of 30mg/kg injected intraperitoneally for 5 days, extract ginseng increased the activity of the basic adenylate cyclase in the brain cortex and decreased the activity of the sodium fluorine (NaF) stimulated enzyme. In a dose of 200mg/kg extract ginseng decreased the activity of both basic and NaF stimulated adenylate cyclase in the brain cortex and in the brain stem. In a dose of 200mg/kg injected intraperitoneally for 5 days extract ginseng lowered the cyclic AMP level in the brainstem and did not change it in the brain cortex. Extract ginseng applied in an oral dose of 30mg/kg for 5 days facilitated the 14C-phenylalanine transport across the blood-brain barrier. On 5 day intraperitoneal injection of extract ginseng (50mg/kg) the amount of free inorganic phosphorus in the brain cortex and the liver increased. 28 references. (Author abstract modified)

003045 Pettigrew, John D.; Kasamatsu, Takuji. Beckman Laboratories of Behavioral Biology, California Institute of Technology 216-76, Pasadena, CA 91125 **Local perfusion of noradrenaline maintains visual cortical plasticity.** Nature (London). 271(5647):761-763, 1978.

The hypothesis that the widespread system of monoaminergic fibers plays a part in regulating plasticity and that catecholamines are responsible for maintaining the high level of plasticity, which is observed in the visual cortex during the critical period, was investigated. A dose and timing regimen of 6-hydroxydopamine to produce significant depletion of catecholamines bilaterally in the visual cortex of 12 developing kittens was developed. Experiments involving microperfusion of catecholamine in localized areas of the visual cortex of animals which could not be expected to show plasticity indicates a specific role of noradrenaline (NA) within the cortex, because plastic changes are found only in the region of cortex perfused by NA, while nearby cortical regions in the same kitten are unaffected. 9 references.

003046 Plenge, Per. Psykokemisk Institut, Kobenhavns Universitet, Rigshospitalet, Blesdamsvej 9, DK-2100 Copenhagen, Denmark **Lithium effects on rat brain glucose metabolism in long-term lithium-treated rats studied in vivo.** Psychopharmacology (Berlin). 58(3):317-322, 1978.

The time course of lithium effects on brain glucose metabolism was investigated in female Wistar rats injected once daily with lithium chloride or saline for 15 days. Animals were killed by freezing in liquid nitrogen 1-8 hours after the last injection. The effect of lithium was most marked during the period in which brain lithium concentration was increasing; the effect wore off as lithium concentration stabilized, even though the stabilized lithium concentration was higher than that which caused maximum effect. Results suggest that lithium effects on several paparmeters of brain glucose metabolism are dependent on the increase in lithium concentration following administration rather than on the absolute concentration of lithium. 21 references. (Author abstract modified)

003047 Poddar, M. K.; Mitra, G.; Ghosh, J. J. Department of Biochemistry, University College of Science, Calcutta University, 35 Ballygunge Circular Road, Calcutta-700 019, India **Delta9-tetrahydrocannabinol-induced changes in brain ribosomes.** Toxicology and Applied Pharmacology. 46(3):737-757, 1978.

The effect of delta9-tetrahydocannabinol (THC) on the stability of rat brain cortex and hypothalamic ribosomes was examined. Under both in vitro and in conditions, THC did not significanly alter the chemical composition and ultraviolet absorption characteristics of the brain cortex and hypothalamus. At low doses (2mg/kg in vivo, 0.2and 0.5mg/g of in vitro), the ribosomal particles were less susceptible to breakdown and the ribosomal ribnucleic acids (RNAs) had a greater proportion of hydro-

gen bonded structure than those of the corresponding control tissues. At high doses (10 and 50mg/kg in vivo, 1.0and 5.0mg/g of tissue in vitro) and under chronic treatment with THC (10mg/kg/day for 21 days), the rebosomal particles became more suscpetible to breakdown with release of protein, RNA, and acid soluble nucleotides than the ribosomes of controls and had a smaller proportion of hydrogen bonded structures than the ribosonal RNAs of control brain cortex and hypothalamus. These differential dose related effects of the THC are ascribed to the difference in degree and mode of hydrophobic interaction between the THC molecule and the ribosomal components. 50 references. (Author abstract modified)

003048 Pong, S. F.; Graham, L. T. Norwich Pharmacal Company, Norwich, N.Y. 13815 **Effect of strychnine on the rat electroretinogram.** Journal of Pharmacy and Pharmacology (London). 30(5):327-328, 1978.

The dose dependent time course effect of strychnine on the amplitude of the b-wave or the rat electroretinogram (ERG) in response to a constant light stimulus is studied. Results indicate a possible beneficial effect of strychnine in amblyopia. Effect of strychnine on the b-wave amplitude was apparently dose dependent. Strychnine either maintained the b-wave amplitude twice that of the control at low dose, or decreased the a-like wave threshold approximately three orders of magnitude in response to a low intensity flash stimuli at high dose. The overall effect is to increase the retinal sensitivity in response to light. 9 references.

003049 Potvin, Barry W.; Stern, Harvey J.; May, S. Randolph; Lam, George F.; Krooth, Robert S. Department of Human Genetics and Development, College of Physicians and Surgeons, Columbia University, New York, NY 10032 **Inhibition by barbituric acid and its derivatives of the enzymes in rat brain which participate in the synthesis of pyrimidine ribotides.** Biochemical Pharmacology (Oxford) 27(5):655-665, 1978.

Barbituric acid was found to be a competitive inhibitor of dihydro-orotate dehydrogenase, uridine phosphorylase, and orotate phosphoribosyltransferase in brain extracts from adult male Wistar rats. The ribotide of barbituric acid, 6-hydroxyuridine-5'-monophosphate, inhibited uridine monophosphate kinase and was a powerful competitive inhibitor of orotidylate decarboxylase, the final enzyme in the de novo synthesis of pyrimidine ribotides. Barbituric acid caused marked competitive inhibition of decarboxylase activity when the reaction mixture contained 5-phosphoribosyl-1-pyrophosphate (PRPP). Phenobarbital, a barbituric acid derivative, was a weak noncompetitive inhibitor of the decarboxylase in the presence of PRPP. Isobarbituric acid, the convulsant barbiturate 5-(1,3-dimethylbutyl)-5-ethyl-barbituric acid, and the stimulatn bemegride (which structurally resembles the barbiturates) inhibited rat brain uridine phosphorylase activity. 50 references. (Author abstract modified)

003050 Prozialeck, Walter C.; Boehme, D. H.; Vogel, Wolfgang H. Dept. of Pharmacology, Thomas Jefferson University, 1020 Locust Street, Philadelphia, PA 19107 **The fluorometric determination of 5-methoxytryptamine in mammalian tissues and fluids.** Journal of Neurochemistry (Oxford). 30(6):1471-1477, 1978.

Using a sensitive and specific fluorometric procedure involving selective extraction, reaction of 5-methoxytryptamine (5-MT) extracts with o-phthalaldehyde (OP) was measured and a determination of 5-MT fluorescent characteristics and intensities was made. Experiments focused on 5-MT in various central and peripheral tissues and fluids of the rat, dog, baboon, and man. Distribution of 5-MT in peripheral tissues of the rat seemed to parallel that of 5-hydroxytryptamine (5-HT), with highest levels being found in the gastrointestinal (GI) tract and Harderian gland, regions that are rich in 5-HT and have been reported to contain systems capable of methylating 5-HT. 5-MT was detected in the lung, plasma, kidney, spleeh, and heart of the rat. 5-MT was present in the CNS of all species examined. No marked interspecies differences were observed. In the rat CNS, the regional distribution of 5-MT did not parallel that of 5-HT, indicating that the systems for the synthesis, uptake, or transport of 5-MT might be different than those for 5-HT. Pretreatment of rats with iproniazid resulted in a 50% increase in whole brain 5-MT. Reserpine pretreatment had no effect, indicating that the storage or release mechanisms for 5-MT are different than for the conventional amine transmitters. 5-MT was detected in human CSF and urine but not in plasma. These data indicate that 5-MT, a compound with potent pharmacological properties, is more widely distributed in the mammalian body than had previously been supposed. 36 references. (Author abstract)

003051 Puri, Surendra K.; Choma, Paul; Volicer, Ladislav. Department of Pharmacology and Experimental Therapeutics, Boston University School of Medicine, Boston, MA 02118 **Cyclic nucleotide levels in the rat striatum and cerebellum -- in vivo effects of dopamine and acetylcholine receptor agonists and antagonists.** Biochemical Pharmacology (Oxford). 27(19):2333-2336, 1978.

The role of dopamine and acetylcholine receptors in the regulation of cyclic nucleotide levels in the striatum and cerebellum was investigated in male Sprague-Dawley rats. Apomorhine increased cyclic adenosine monophosphate levels only in the striatum, and this effect was blocked by haloperidol and dexetimide. Cyclic guanosine monophosphate (GMP) levels were increased both in the striatum and cerebellum by apomorphine and pilocarpine. Haloperidol significantly decreased cyclic GMP levels and blocked the effect of apomorphine and pilocarpine on cyclic GMP in the cerebellum. In the striatum, haloperidol blocked only the pilocarpine-induced rise of GMP. Dexetimide increased cyclic GMP levels and failed to block the rise in cyclic GMP induced by apomorphine or pilocarpine. Results suggest that the regulation of cyclic GMP levels may involve more than one mechanism. 30 references. (Author abstract)

003052 Puri, Surendra K.; Spaulding, Theodore C.; Mantione, Charles R. Hoechst-Roussel Pharmaceuticals Inc., Route 202-206 North, Somerville, NJ 08876 **Dopamine antagonist binding: a significant decrease with morphine dependence in the rat striatum.** Life Sciences (Oxford). 23(6):637-641, 1978

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New BiochemicalApproaches, held in Beerse, Belgium, July 1978, changes in the sensitivity of dopamine receptors in morphine dependent Sprague-Dawley rats are reported. Acute morphine (intraperitoneal injection of 30mg/kg) did not alter 3H-spiroperidol specific binding in striatal tissue. However, rats made dependent on morphine with two 50mg pellets showed significantly decreased binding and increased dissociation constants (Kd) when withdrawn for 24 or 48 hours. Binding sites were reduced with a decrease in Kd in rats implanted with four 50mg pellets or receiving high doses of morphine. Results indicate that binding characteristics of 3H-spiroperidol depend on the relative dose of morphine used to induce dependence. Low dose dependence results in a decrease in binding affinity, while high dose dependence results in an increase of 3H-spiroperidol affinity in the presence of fewer binding sites. 20 references. (Author abstract modified)

003053 Pycock, Christopher; Horton, Roger. Department of Pharmacology, Medical School, University of Bristol, Bristol, BS8 1TD, England **Regional changes in the concentrations of cerebral monoamines and their metabolites after ethanolamine-O-**

sulphate-induced elevation of brain gamma-aminobutyric acid concentrations. Biochemical Pharmacology (Oxford). 27(14):1827-1830, 1978.

The effects of ethanolamine-O-sulphate-induced elevation of cerebral gamma-aminobutyric acid (GABA) concentrations on the levels of norepinephrine (NE), dopamine (DA), 5-hydroxytryptamine (5-HT) and their metabolites in the Sprague-Dawley rat brain were investigated. Increased GABA concentrations were associated with a decrease in DA turnover in limbic regions, but striatal DA was not significantly affected. Increased cerebral GABA concentrations also resulted in increased 5-HT turnover in some brain regions but had no effect on regional NE turnover. Possible sites of interaction between the neurotransmitters are discussed. 29 references. (Author abstract modified)

003054 Quach, T. T.; Rose, C.; Schwartz, J. C. Unite 109 de Neurobiologie, Centre Paul Broca de l'INSERM, 2er, rude d'Alesia, F-75014 Paris, France **(3H)Glycogen hydrolysis in brain slices: responses to neurotransmitters and modulation of noradrenaline receptors.** Journal of Neurochemistry (Oxford). 30(6):1335-1341, 1978.

A study of the responses to neurotransmitters and the modulation of noradrenaline receptors by (3H)glycogen hydrolysis in mouse cortical slices was conducted and noradrenaline, serotonin, and histamine were found to induce clear concentration dependent glycogenolysis. (3H)Glycogen hydrolysis induced by noradrenaline appears to be mediated by beta-adrenergic receptors because it is completely prevented by timolol, while phentolamine is ineffective. It seems to involve cyclic AMP because it is potentiated in the presence of isobutylmethylxanthine; in addition dibutyryl cyclic AMP (but not dibutyryl cyclic GMP) promotes glycogenolysis. Lower concentrations of noradrenaline were necessary for (3H)glycogen hydrolysis than for stimulation of cyclic AMP accumulation. After subchronic reserpine treatment the concentration response curve to noradrenaline was significantly shifted to the left without modifications of either the basal (3H)glycogen level, maximal glycogenolytic effect, or the dibutyryl cAMP-induced glycogenolytic response. In addition to noradrenaline, clear concentration dependent (3H)glycogen hydrolysis was observed in the presence of histamine or serotonin. In contrast to the partial (3H)glycogen hydrolysis elicited by these biogenic amines, depolarization of the slices by 50mM K provoked a nearly total (3H)glycogen hydrolysis. 20 references. (Author abstract)

003055 Quattrone, A.; Crunelli, V.; Samanin, R. Istituto di Ricerche Farmacologiche "Mario Negri," Via Eritrea 62, I-20157 Milan, Italy **Seizure susceptibility and anticonvulsant activity of carbamazepine, diphenylhydantoin and phenobarbital in rats with selective depletions of brain monoamines.** Neuropharmacology (Oxford). 17(8):643-647, 1978.

The effects of selective lesioning of brain monoamine containing neurons on electroshock seizure thresholds and on anticonvulsant activity of diphenylhydantoin, phenobarbital, and carbamazepine were studied in female rats. Intraventricular injection of 6-hydroxydopamine (6-OHOA), which markedly decreased brain catecholamine concentrations, lowered seizure thresholds and decreased drug anticonvulsant effects. Pretreatment with desipramine, which protected adrenergic neurons from the neurotoxic action of 6-OHDA, did not significantly affect seizure thresholds and drug activity with respect to controls. Raphe lesions, which selectively decreased brain serotonin, did not significantly affect seizure thresholds and drug anticonvulsant activity. Results are compatible with the hypothesis that brain catecholamines, particularly noradrenaline, play a role in the control of seizure activity and in the anticonvulsant activity of diphenylhydantoin, phenobarbital, and carbamazepine in the rat. 35 references. (Author abstract modified)

003056 Quik, Maryka; Iversen, Leslie L.; Bloom, Stephen R. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Hills Road, Cambridge, England **Effect of vasoactive intestinal peptide (VIP) and other peptides on cAMP accumulation in rat brain.** Biochemical Pharmacology (Oxford). 27(18):2209-2213, 1978.

The effects of several brain peptides on adenylate cyclase activity in male Sprague-Dawley rat brain homogenates and on cyclic adenosine monophosphate (AMP) and cyclic guanosine monophosphate (GMP) levels in brain slices were determined. Substance-P, luteinizing hormone releasing factor, thyrotropin releasing factor, somatostatin, glucagon, and neurotensin were without effect in these tests. When slices from a number of brain regions were incubated with 0.5mcM vasoactive intestinal peptide (VIP), a significant increase in the accumulation of cyclic AMP was observed; there were no changes in cyclic GMP levels. VIP also caused an increase in cell free adenylate cyclase activity of striatal, cortical, and hippocampal homogenates and slices; these increases were calcium dependent in cortical and hippocampal slices but not in striatal slices. When tissue slices were incubated with VIP and a variety of antagonist drugs, no alteration in the VIP-induced increase in cyclic AMP was observed. When VIP was incubated with other agents known to stimulate adenylate cyclase activity, the increases in cyclic AMP levels were additive. Results suggested that VIP acts as a neuromodulatory or neurotransmitter compound in the CNS, mediating its action through the adenylate cyclase/cyclic AMP system. 35 references. (Author abstract modified)

003057 Quock, Raymond M.; Weick, Barton G. Department of Physiology-Pharmacology, School of Pharmacy, University of the Pacific, Stockton, CA 95211 **Tryptamine-induced drug effects insensitive to serotoninergic antagonists: evidence of specific tryptaminergic receptor stimulation?** Journal of Pharmacy and Pharmacology (London). 30(5):280-283, 1978.

A study was made to: 1) compare the effects of tryptamine and 5-hydroxytrptophan (5-HTP) in the rabbit hypothermia model, and 2) determine whether the thermotropic effects of tryptamine might be explained by an interaction with serotoninergic receptors. Both agents evoked hyperthermia and behavioral excitation; tryptamine but not 5-HTP also produced forepaw clonic activity. Serotoninergic receptor blockers abolished the effects of 5-HTP, but only weakly influenced tryptamine responses. Both tryptamine and 5-HTP effects were potentiated by fluoxetine. Methergoline, a putative tryptaminergic receptor blocker, antagonized tryptamine-induced hyperthermia and forepaw clonus but did not influence 5-HTP responses. It is postulated that while 5-HTP produces its effects through a serotoninergic mechanism, some of the responses to tryptamine result from activation of a specific tryptamine- sensitive mechanism. 30 references. (Author abstract modified)

003058 Ramsey, Robert B. Department of Neurology, St. Louis University School of Medicine, St. Louis, MO 63104 **Effect of hypocholesterolemic agents on central nervous system cholesterol biosynthesis. III. Zuclomiphene in combination with AY9944 and triparanol.** Biochemical Pharmacology (Oxford). 27(12):1637-1640,1978.

Treatment of developing Wistar rats with a combination of hypocholesterolemic agents (zuclomiphene, triparanol, and AY9944) resulted in the accumulation of delta7 sterols and abnormal levels of desmoterol and zymosterol in the brain. Pretreatment with the hypocholesterolemic agents followed by intracerebral injection of (2-14C)mevalonic acid yielded compara-

ble labeling of free sterols in treated and control animals. A significant increase in the labeled squalene oxide/steryl ester fraction derived from the brains of animals treated with the hypocholesterolemic agents was observed, accompanied by a significant decrease in labeled cholesterol. Examination of the labeled free sterol fraction by silver nitrate impregnated thin layer chromatography and radioactivity monitored gas/liguid chromatography indicated that sterol biosynthesis was impeded in the brains of treated animals. An increase in labeled sterols with a C-4 methyl group and elevated (14C)cymosterol was also observed in animals treated with the hypocholesterolemic agents. 21 references. (Author abstract modified)

003059 Randic, Mirjana; Miletic, Vjekoslav. Department of Veterinary Anatomy, Pharmacology, and Physiology, Iowa State University of Science and Technology, Ames, IA 50011 **Depressant actions of methionine-enkephalin and somatostatin in cat dorsal horn neurones activated by noxious stimuli.** Brain Research (Amsterdam). 152(1):196-202, 1978.

Somatostatin and methionine-enkephalin were applied microiontophoretically to dorsal horn nocioceptive neurons and to units activated by sensitive mechanoreceptors in cats. Both peptides showed selective depressant activities on the excitability of nociceptive dorsal horn neurons located in laminae 1, 2, and 5. In contrast, the majority of units excited by sensitive mechanoreceptors were either not affected or occasionally weakly excited by these peptides. Naloxone antagonized the methionine-enkephalin depression in all nocioceptive neurons but did not affect responses of units excited by sensitive mechanoreceptors. Somatostatin depression of nocioceptive units was not modified by naloxone. The reversal of the depressant effect of methionine-enkephalin by naloxone indicates that this peptide was probably acting on specific opiate receptors. 31 references.

003060 Rangaraj, Narayan; Kalant, Harold. Department of Pharmacology, University of Toronto, Ontario, Toronto, Canada M5S 1A8 **Effects of ethanol withdrawal, stress and amphetamine on rat brain (Na K)-ATPase.** Biochemical Pharmacology (Oxford). 27(8):1139-1144, 1978.

Adenosine triphosphatase (ATPase) activity was studied in brain preparations from male Wistar rats at various times after acute and chronic administration of ethanol, after acute treatment with amphetamine, and after hyeractivity in the form of forced swimming. In rats fed ethanol up to the time of sacrifice, ethanol caused no increase in Na/K ATPase activity of whole brain homogenates. Activity was increased during the period 12-48 hours after withdrawal of ethanol, however, and was greatest at 24 hours. Fractionation of the homogenate showed that the increase was confined to the lysed synaptosomal fraction. Activity was also increased at 16 hours after one acute dose of ethanol (5g/kg). The increased ATPase activity during withdrawal could be blocked by administration of another dose of ethanol one hour before sacrifice, in both acutely and chronically ethanol treated rats. ATPase activity was also increased by amphetamine in a dose dependent manner, both in vivo and vitro, and by forced swimming. In the rise in ATPase activity during ethanol withdrawal is considered an activation by conformation change, secondary to catecholamine release due to stress. 40 references. (Author abstract modified)

003061 Rao, S. L. N. Nutrition Section, Hindustan Lever Ltd., Andheri East, Bombay, India **Entry of beta-N-oxalyl-L-alpha,beta-diaminopropionic acid, the Lathyrus sativus neurotoxin into the central nervous system of the adult rat, chick and the rhesus monkey.** Journal of Neurochemistry (Oxford). 30(6):1467-1470, 1978.

A comparative study of the tissue disposition of the Lathyrus sativus neurotoxin was done using beta-N-oxalyl-L-alpha, beta-diaminopropionic acid (3H)ODAP) with special reference to the CNS in normal and Diamox treated (acidotic) adult rhesus monkeys and also in the day old chick, a species susceptible to the neurotoxin, and the adult rat, which is refractory to it. The neurotoxin was detected in the CNS of the acidotic monkey and also in the normal monkey in nearly the same quantity. The neurotoxin was largely localized in the lumbosacral region of the spinal cord. The amount of radioactive ODAP in the CNS following its intraperitoneal injection was twice that seen following its intravenous injection. The concentrations of the neurotoxin 90 min after injection in the CNS of the adult rat and the day old chick were almost the small and increased two fold by 24 hr. No radioactive metabolite of ODAP could be detected in either the tissues or the urine of the different species. Species (and age) differences in susceptibility to the Lathyrus sativus neurotoxin is thus independent of its entry into the CNS. 23 references. (Author abstract)

003062 Rastogi, R. B.; Singhal, R. L. Department of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada **Evidence for the role of adrenocortical hormones in the regulation of noradrenaline and dopamine metabolism in certain brain areas.** British Journal of Pharmacology (London). 62(1):131-139, 1978.

The influence of bilateral adrenalectomy (BA) on the biosynthetic capacity for catecholamines in brain tissue was studied in male Sprague-Dawley rats. BA suppressed body growth and increased the activity of tyrosine hydroxylase (TH) in rat striatum in a time dependent manner. Fifteen days after BA, the concentrations of noradrenaline (NA) were decreased significantly in hypothalamus and striatum, as were those of dopamine (DA) in brain stem and striatum. Catechol-O-methyltransferase failed to change in response to BA, but the activity of monoamine oxidase (MAO) in cortex as significantly parameters were even more pronounced 15 days after adrenal ablation. Administration of corticosterone (10mg/kg i.p.)to the adrenalictomized rats effectively reversed the observed effects on brain amine metabolism. Corticosterone treatment for 7 days beginning from the 8th day of adrenalectomy virtually restored the concentrations of NA and DA as well as the activities of striatal TH and cerebrocortical MAO to the values seen for sham operated controls. Changes seen in brain NA and DA of adrenalectomized rats are probably specific to adrenocortical steroids; the data further suggest that these hormones play a role in the regulation of catecholamine formation. 34 references. (Author abstract modified)

003063 Reches, A.; Ebstein, R. P.; Belmaker, R. H. Jerusalem Mental Health Center-Ezrath Nashim, P.O.B. 140, Jerusalem, Israel **The differential effect of lithium on noradrenaline- and dopamine-sensitive accumulation of cyclic AMP in guinea pig brain.** Psychopharmacology (Berlin). 58(2):213-216, 1978.

The effect of lithium in its narrow therapeutic concentration range on noradrenaline (NA) sensitive and dopamine (DA) sensitive accumulation of cyclic adenosine monophosphate (AMP) was studied in vitro in the guinea pig brain. Therapeutic concentrations of lithium inhibited NA sensitive but not DA sensitive accumulation of cyclic AMP. Results suggest a pharmacological distinction between the antischizophrenic drugs that inhibit DA sensitive cyclic AMP accumulation and lithium, an antimanic agent that specifically inhibits only the NA sensitive cyclic AMP accumulation. 28 references. (Author abstract modified)

003064 Richelson, Elliot; Prendergast, Franklyn G.; Divinetz-Romero, Silvia. Department of Psychiatry, Mayo Foundation,

Rochester, MN 55901 **Muscarinic receptor-mediated cyclic GMP formation by cultured nerve cells -- ionic dependence and effects of local anesthetics.** Biochemical Pharmacology (Oxford). 27(16):2039-2048, 1978.

A new assay technique for measuring receptor mediated cyclic guanosine monophosphate (GMP) formation by cultured mouse neuroblastoma cells was used to study the ionic requirements of the muscarinic receptor and the effect of local anesthetics on receptor function. The technique involved radioactively labeling intracellular stores of guanosine triphosphate (GTP) by incubating cells with (3H)guanine and isolating (3H)cyclic GMP with a cation exchange resin column. High pressure liquid chromatography of cell extracts and eluates from the column showed that after 45 minutes the majority of the radioactivity in the cell extracts was (3H)GTP, and for carbamylcholine stimulated cells, greater than 90% of the radioactivity in the eluates was (3H)cyclic GMP. In the absence of external sodium ions or external calcium ions, the carbamylcholine stimulated formation of (3H)cyclic GMP was about 60% and 10% of control, respectively, while removal of other ions had no significant effect. Local anesthetics were apparently competitive inhibitors of carbamylcholine with equilibrium dissociation constants in the range of 6-250mcM. Tetracaine, butacaine, and procaine showed greatest apparent affinity for the muscarinic receptor. Ethyl aminobenzoate showed the least receptor affinity, while dibucaine and lidocaine had intermediate affinity values. 55 references. (Author abstract modified)

003065 Riddall, Dieter R.; Leavens, William J. Department of Pharmacology, Wellcome Research Laboratories, Langley Court, Beckenham, Kent, BR3 3BS England **Affinities of drugs for the agonist and antagonist states of the dopamine receptor.** European Journal of Pharmacology (Amsterdam). 51(2):187-188, 1978.

The potencies of several dopamine agonists and antagonists in displacing (3H)-apomorphine and (3H)-spiroperidol binding were investigated in calf caudate membranes. Dopamine agonists and neuroleptics showed a wide range of affinities for the two ligand binding sites. Bromocriptine was 2.3times more potent as an antagonist than as an agonist. Fluspirilene showed little or no affinity for (3H)-apomorphine binding sites and was more specific than chlorpromazine, haloperidol, or spiroperidol for the antagonist state of the dopamine receptor, as defined by (3H)-spiroperidol binding. 5 references.

003066 Robertson, H.A.; Martin, I.L.; Candy, J.M. Department of Pharmacology, Dalhousie University Medical School, Halifax, Nova Scotia, Canada B3H 4H7 **Differences in benzodiazepine receptor binding in Maudsley reactive and Maudsley non-reactive rats.** European Journal of Pharmacology (Amsterdam). 50(4):455-457, 1978.

The distribution of benzodiazepine receptors was investigated in two strains of rats selectively bred for high and low fearfulness, the Maudsley reactive (MR) and Maudsley nonreactive (MNR) strains. In every brain region examined, the MNR animals showed higher specific benzodiazepine binding than the MR animals, although this difference attained statistical significance only in the hippocampus, hypothalamus, midbrain, medulla/pons, and spinal cord. Scatchard analyses on midbrain/hypothalamus tissue indicated dissociation constant values of 3.64nmol in MR animals and 3.24nmol in MNR rats. The total number of binding sties was 1000fmol/mg protein in MR rats and 1385fmol/mg protein in MNR rats. The differences in the density of benzodiazepine receptors in two rat strains that differ in emotional reactivitiy may provide a biological basis for investigations of emotional behavior. 5 references.

003067 Roby, Arthur; Orzechowski, Raymond F. Department of Biological Sciences, Philadelphia College of Pharmacy and Science, Philadelphia, PA 19104 **Selective blockade of dopamine-induced vasodilation by ergonovine maleate in the vasculatures of dogs and rabbits.** Research Communications in Chemical Pathology and Pharmacology. 19(2):243-256, 1978.

The effects of ergonovine on dopaminergic vasodilation in dog and rabbit vasculatures were compared to ergonovine's effects upon vasodilator responses evoked by acetylcholine and isoproterenol. In urethane anesthetized rabbits, ergonovine maleate significantly attenuated dopamine-induced systemic hypotension. Initial pressor responses to dopamine were significantly prolonged and potentiated by ergonovine. Mesenteric vasodilation elicited by dopamine in dogs was competitively inhibited by ergonovine at doses of 0.09 and 0.18 mg/kg, intraperitoneally. Failure of ergonovine to inhibit vasodilatory responses to acetylcholine or isoproterenol suggests a selective blockade. These results confirm existing evidence that ergonovine selectively antagonizes peripheral dopaminergic receptors subserving vasodilation. 7 references. (Author abstract)

003068 Roel, L. E.; Levine, P.; Rubin, D.; Markovitz, D.; Munro, H. N.; Wurtman, R. J. Department of Psychiatry, University of California at San Diego Medical School M-003, La Jolla, CA 92093 **Effect of L-DOPA pretreatment on in vivo protein synthesis in various rat brain regions.** Life Sciences. 22(21):1887-1892, 1978.

A single intraperitoneal dose of L-dihydroxyphenylalanine (L-dopa, 500mg/kg) caused massive disaggregation of brain polysomes and suppressed the incorporation of (3H)lysine into trichloracetic acid precipitable proteins of cortex, cerebellum, hypothalamus, brainstem, and striatum in male Sprague-Dawley rats. The magnitude of the inhibition of (3H)protein synthesis was similar in all brain regions and was not related to changes in the specific activity of the precursor amino acid. 20 references. (Author abstract)

003069 Rokyta, R.; Chaloupka, Z.; Sobotka, P.; Frankova, S.; Vencovsky, E. Dept. of Pathological Physiology, Medical Faculty, Charles University, Lidicka 1, Plzen, Czechoslovakia **The effect of cerebrolysine on cortical evoked potentials in rats with early malnutrition.** Activitas Nervosa Superior (Praha). 20(1):83-84, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the effect of cerebrolysine on cortical evoked potentials in rats with early malnutrition is described. The latencies of cortical evoked potentials were prolonged after pentobarbital in all experimental groups. The amplitudes of cortical evoked potentials increased in normally fed saline rats, but in low protein saline rats the amplitude of both the positive and negative wave was diminished after pentobarbital. In rats given cerebrolysine (both normal and undernourished) the positive wave was augmented, while the negative did not change after pentobarbital. 3 references.

003070 Rosecrans, J. A. ; Krynock, G. M.; Newlon, P.; Chance, W. T.; Kallman, M. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Central mechanisms of drugs as discriminative stimuli: involvement of serotonin pathways.** Psychopharmacology (Berlin). 58(2):9, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the role of serotonin (5-HT) systems in the mechanisms of action of lysergic acid diethylamide (LSD) and morphine was reported. The amine systems were manipulated pharmacologically and neurophysiologically in rats trained to discriminate

LSD or morphine using a two lever operant procedure, with a variable interval 15 second schedule of reinforcement. The same procedure was used to evaluate the effects of drugs administered to the periaquaductal gray (PAG). Results indicate that LSD may act by inhibiting presynaptic PAG sites; this effect may reflect LSD agonism at 5-HT receptors located within the PAG. The discriminative stimulus effects of morphine may also reflect an agonist effect at LSD sensitive sites or may involve a different set of 5-HT receptors.

003071 Ross, Svante B.; Renyi, Anna L. Research and Development Laboratories, Astra Lakemedel AB, S-151 85 Sodertalje, Sweden **Effect of ()-amphetamine on the retention of 3H-Catecholamines in slices of normal and reserpinized rat brain and heart.** Acta Pharmacologica et Toxicologica (Kobenhavn). 42(5):328-336, 1978.

The effect of reserpine on the inhibition by ()amphetamine and cocaine of the accumulation of (3H)dopamine (DA) in striatal slices and (3H)noradrenaline (NA) in slices of cerebral occipital cortex and heart atrium of rats, and the release of the (3H)amines from these tissues were examined. Reserpine (5mg/kg intraperitoneally) was injected 18 hours before the experiments. The findings show reserpine markedly enhanced the in vitro potency of amphetamine in the striatum and heart but only slightly in the cortex. After administration in vivo ()amphetamine was about 10 times more potent in reducing the amine accumulation in the cortex than in the striatum. Reserpine enhanced the effect in both regions. The inhibitory potency of cocaine in vitro was unchanged by reserpine in the striatum, but was reduced in the cortex and heart. Reserpine did not change the inhibitory potency of desopramine in the cortex and heart. The release of the (3H)amines by ()amphetamine was enhanced by reserpine in the striatum and heart, but the small release produced in the cortex was not increased. The release produced by cocaine was similarly enhanced by reserpine, but cocaine was much less active than ()amphetamine. Results indicate that ()amphetamine and cocaine inhibit the amine accumulation by different mechanisms. 15 references. (Author abstract)

003072 Rotsztejn, William H.; Drouva, Sophia V.; Pattou, Eliane; Kordon, Claude. Unite 159 de Neuroendocrinologie, Centre Paul Broca de l'INSERM, 2ter rue d'Alesia, F-75014 Paris, France **Effect of morphine on the basal and the dopamine-induced release of LHRH from mediobasal hypothalamic fragments in vitro.** European Journal of Pharmacology (Amsterdam). 50(3):285-286, 1978.

The effects of morphine on the basal and dopamine (DA)-induced release of luteinizing hormone releasing hormone (LH-RH) were investigated in vitro in mediobasal hypothalamic fragments from male Sprague-Dawley rats. The addition of morphine to the incubation medium had no effect on basal LH-RH release from the palisadic zone of the median eminence (PZ) or the infundibular sulcus(IS). In contrast, DA significantly increased the amount of LH-RH release from the PZ but not from the IS; this effect was abolished when morphine was added to the incubation medium. Naloxone reversed the inhibitory effect of morphine on DA-induced LH-RH secretion from the PZ. Thus, morphine had no effect itself on the basal secretion of LH-RH from the median eminence, but interfered with the capacity of neurosecretory endings to respond to DA stimulation. Results suggest that an interaction with DA receptors located on LH-RH neurosecretory neurons in the median eminence may account for the effects of morphine on gonadotropin secretion. 5 references.

003073 Sakurada, Osamu; Sokoloff, Louis; Jacquet, Yasuko F. Laboratory of Cerebral Metabolism, NIMH, Bethesda, MD 20014 **Local cerebral glucose utilization following injection of beta-endorphin into periaqueductal gray matter in the rat.** Brain Research (Amsterdam). 153(2):403-407, 1978.

The (14C)deoxyglucose method was used to determine the metabolic rates of different regions of the CNS during a state of catatonia and sedation induced by local microinjection of beta-endorphin into the periaqueductal gray matter (PAG) of male Sprague-Dawley rats. Injection of 4-8mcg of beta-endorphin into the PAG resulted in a generalized decrease in glucose utilization throughout the brain, reflecting a diffuse depression of cerebral functional activity. This pervasive, long-acting effect of miniscule amounts of beta-endorphin argues for a potent neuromodulatory rather than a direct neurotransmitter role for this opioid peptide. Available evidence suggests that the direct and indirect action of the endorphin receptor is primarily an inhibitory one. 15 references.

003074 Samanin, R.; Quattrone, A.; Peri, G.; Ladinsky, H.; Consolo, S. Clinica Neurologica, Universita di Messina, Messina, Italy **Evidence of an interaction between serotoninergic and cholinergic neurons in the corpus striatum and hippocampus of the rat brain.** Brain Research (Amsterdam). 151(1):73-82, 1978.

The interaction between serotoninergic and cholinergic neurons in the brain was investigated by studying the effects of quipazine and D-fenfluramine on regional brain acetylcholine in rats. Quipazine (10 mg/kg) significantly increased the levels of acetylcholine in the striatum and hippocampus but not in the Telencephalon and brain stem. The increase was not significantly modified by electrolytic lesions placed in the midbrain raphe nuclei. Pretreatment with serotonin antagonists prevented the increase induced by quipazine. The quipazine-induced increase in hippocampal acetylcholine was blocked by an electrolytic lesion of the nucleus medianus raphe. D-Fen Fluramine also significantly increased striatal acetylcholine, its effect being completely prevented by p-chlorophenylaline pretreatment. Findings are compatible with the hypothesis that serotoninergic neurons originating in the raphe nuclei may normally serve to inhibit cholinergic neurons in two area of the rat brain. 36 references. (Author abstract modified)

003075 Sargent, Thornton, III; Braun, Gisela; Braun, Ulrich; Budinger, Thomas F.; Shulgin, Alexander T. Donner Laboratory and Lawrence Berkeley Laboratory, University of California, Berkeley, CA 94720 **Brain and retina uptake of a radioiodine labeled psychotominetic in dog and monkey.** Communications in Psychopharmacology. 2(1):1-10, 1978.

4-Iodo-2, 5-dimethoxyphenylisopropylamine (4-I-DPIA), a close analog of methoxylated psychotomimetic compounds, was prepared with iodine isotopes 131I and with 123I and its distribution studied in the dog and monkey using-imaging devices of nuclear medicine. Images were obtained showing isotope accumlation in the brain and eyes in both animals; the measured uptake half time in the monkey brain was 8sec. Sacrifice and dissection of the dogs showed 2% of the activity in the brain. 18% in the liver, and 12% in the lung. The concentration in retina was five times that in any other central nervous system-tissue, supporting the concept that direct action at the retinal level is a component of visual misperception caused by psychotomimetics. 17 references. (Author abstract modified)

003076 Sastry, B. R. Department of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, S7N 0W0, Canada **Morphine and met-enkephalin effects on sural Adelta afferent terminal excitability.** European Journal of Pharmacology (Amsterdam). 50(3):269-273, 1978.

The effects of morphine and metenkephalin on the excitability of cutaneous afferent terminals were studied. Morphine (30-80nA) and met-enkephalin (30-80nA) decreased the excitability

of single sural Adelta afferent terminals and potentiated the enhancement of the terminal excitability produced by superficial peroneal nerve stimulation in midcollicular decerebrate and spinalized cats. Naloxone (20-40nA) antagonized the actions of both substances on the unconditioned and conditioned terminal exitabilities. Results indicate that morphine and met-enkephalin hyperpolarize Adelta sural afferent terminals and facilitate the terminal depolarization during presynaptic inhibition. This enhancement of presynaptic inhibition may be partially responsible for the analgesic action of these agents. 10 references. (Author abstract modified)

003077 Schmidt, D. E.; Buxbaum, D. M. Tennessee Neuropsychiatric Institute, Vanderbilt University School of Medicine, Nashville, TN 37240 **Effect of acute morphine administration on regional acetylcholine turnover in the rat.** Brain Research (Amsterdam). 147(1):194-200, 1978.

The effects of morphine administration on regional acetycholine (ACh) turnover were determined in male Sprague-Dawley rats treated with hemicholinium-3 (HC-3), an ACh synthesis blocker. Since morphine administration did not alter ACh levels, the rate of decline of ACh following morphine plus HC-3 was compared directly with HC-3 control values. Morphine did not cause significant changes in ACh turnover in the striatum at any dose. A significant decline in ACh turnover in the hypothalamus and hippocampus occurred following doses of morphine of 4mg/kg and higher. In the midbrain, a dose of 16 mg/kg or higher was required to produce a significant decline in AChturnover. The decline in ACh turnover in the hippocampus and hypothalamus at 1 hour after administration of morphine was reversed within 3 hours, while ACh turnover in the midbrain remained significantly depressed for 5 hours. These findings are in agreement with data previously obtained from isotopic studies of the effects of morphine on regional ACh turnover. The importance of using both isotopic and HC-3 methods in measuring ACh turnover is discussed. 25 references.

003078 Schumann, Alan Martin. Virginia Commonwealth University/Medical College of Virginia **The effects of inorganic lead on the central catecholaminergic system of the rodent with emphasis on postnatally exposed rats and mice. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. Mfilms, No. 7732898, HC$15. MF$7.50. 163 p. 1977.

Newborn mice and rats were experimented upon to determine the effects of inorganic lead on the functional activity of central catecholaminergic neurons by assessing the rate of formation of the hypothesized functional pool of newly synthesized, preferentially released 3H-norepinephrine (3H-NE) and 3H-dopamine (3H-DA) synthesized from 3H-tyrosine. In all cases, the lead intoxicated pups had reduced body weights compared to untreated controls. Lead acetate failed, however, to significantly alter the endogenous levels of tyrosine, NE or DA, or the rate of formation 3H-NE and 3H-DA compared to pair fed controls. The lead intoxicated rodents were not hyperactive compared to pair fed controls. Results indicate that the central catecholaminergic system of the postnatal rodent is resistant to the effects of inorganic lead when assessed on whole brain level. (Journal abstract modified)

003079 Schwabe, Ulrich; Ohga, Yuzo; Daly, John W. National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH, Bethesda, MD 20014 **The role of calcium in the regulation of cyclic nucleotide levels in brain slices of rat and guinea pig.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 302(2):141-151, 1978.

The chelating agent ethylene-bis-(beta-aminoethyl ether)-N,N'-tetraacetic acid (EGTA) was used to determine the role of extracellular calcium in hormone elicited accumulations of cyclic adenosine monophosphate (AMP) in rat and guinea pig cortical slices. In rat cerebral cortical slices, the addition of EGTA to acutely lower extracellular calcium concentrations greatly reduced the accumulation of cyclic AMP elicited by norepinephrine (NE) but had little effect on the response to adenosine or N6-phenylisopropyladenosine. Addition of EGTA in guinea-pig slices increased basal levels of cyclic AMP and the response to NE, adenosine, and phenylisopropyladenosine. The response to histamine was unchanged. Results indicate that the presence of extracellular calcium is critical for NE and histamine elicited accumulations of cyclic AMP in brain slices but not for responses to adenosine. Released adenosine can, at least partially, substitute for extracellular calcium in maintaining responsiveness of amine sensitive cyclic AMP generating systems in brain slices. 41 references. (Author abstract modified)

003080 Schwarcz, Robert; Creese, Ian; Coyle, Joseph T.; Snyder, Solomon H. John Hopkins University School of Medicine, Baltimore, MD 21205 **Dopamine receptors localised on cerebral cortical afferents to rat corpus striatum.** Nature (London). 271(5647):766-768, 1978.

The effects of selective degeneration of striatal intrinsic neurones with the neurotoxin, kainic acid, and elimination of cortico/striate afferents by cortical ablation on the dopamine receptors in rat striatum were investigated. Kainate induced changes in dopamine sensitive adenylate cyclase and H-haloperidol binding differ both in extent and in time course. Observations indicate a clear dissociation between the activity of dopamine sensitive adenylate cyclase and H-haloperidol binding sites in the striatum. It is concluded that a substantial portion of striatal H-haloperidol receptor sites are localized to axons of cerebral cortical afferents whereas dopamine sensitive adenylate cyclase is confined to neurones intrinsic to the striatum. 17 references.

003081 Schwarcz, Robert; Zaczek, Robert; Coyle, Joseph T. Coyle: Department of Pharmacology, Johns Hopkins University School of Medicine, 725 N. Wolfe Street, Baltimore, MD 21205 **Microinjection of kainic acid into the rat hippocampus.** European Journal of Pharmacology (Amsterdam). 50(3):209-220, 1978.

The morphologic, neurochemical, and behavioral effects of unilateral injection of kainic acid into the hippocampus of Sprague-Dawley rats were investigated. Infusion of 10nmoles of kainate caused a rapid and complete degeneration of neuronal perikarya in the entire hippocampal formation, followed by gliosis and atrophy of the region. The unilateral neuronal loss was accompanied by a 50% decrease in the specific activity of the biochemical markers for gamma-aminobutyric acid (GABA) containing neurons, including glutamic acid decarboxylase, endogenous GABA, and synaptosomal uptake of (3H)GABA. The extrinsic hippocampal cholinergic and noradrenergic afferents also showed significant alteration. Although the specific activity of choline acetyltransferase was unaffected and the specific activity of tyrosine hydroxylase was significantly increased in the injected hippocampus, the synaptosomal high affinity uptake processes for (3H)choline and (3H)norepinephrine were significantly reduced 10 days after injection. The level of endogenous acetylcholine was elevated in the lesioned hippocampus 2 days after injection, but the level of endogenous norepinephrine was reduced. For several hours after intrahippocampal injections of 5nmoles or more of kainate, rats showed epileptiform behavior, suggesting that this may be a useful rodent model for temporal lobe seizure disorders. 35 references. (Author abstract modified)

003082 Segal, M. Isotope Department, Weizmann Institute of Science, Rehovot, Israel **The acetylcholine receptor in the rat hippocampus; nicotinic, muscarinic or both?** Neuropharmacology (Oxford). 17(8):619-623, 1978.

Responses of hippocampal neurons to the iontophoretic application of acetylcholine (ACh) and nicotine were measured in urethane anesthetized male Wistar rats. Most of the bursting type cells were excited by ACh and about half were depressed by nicotine. The excitation was reversed by atropine and in some cases by gallamine. Most of the nonbursting theta cells were depressed by nicotine but unaffected by ACh. The depression was antagonized by d-tubocurarine. It is suggested that the hippocampus contains both muscarinic and nicotinic receptors that have different anatomical distributions and physiological significance. 14 references. (Author abstract)

003083 Semiginovsky, B.; Sobotka, P.; Jakoubek, B. Institute of Pathophysiology, Medical Faculty, Charles University, Pilsen, Czechoslovakia **A contribution to the neurochemical basis of the pyrithioxin effect on the brain glucose utilisation during relative brain hypoglycaemia induced by anticipation stress.** Activitas Nervosa Superior (Praha). 20(1):84-85, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the neurochemical basis of the pyrithioxin effect on brain glucose utilization during relative brain hypoglycemia induced by anticipation stress is discussed. Stress conditions did not significantly change cerebral levels of free amino acids, while during pyrithioxin treatment an increase of beta-alanine, lysine, and ethanolamine content was found in standard rats as well as rats subsequently stressed. Cerebral gamma-aminobutyric acid content was relatively stable in all conditions.

003084 Sethy, Vimala H.; Bombardt, Paul A. Upjohn Company, CNS Research, Kalamazoo, MI 49001 **Is GABA involved in analgesia?** Research Communications in Chemical Pathology and Pharmacology. 19(2):365-368, 1978.

The effect of morphine and naloxone on gamma-aminobutyric acid (GABA) concentration in discrete areas of the rat brain was studied to determine its role in analgesia. Morphine sulfate and naloxone hydrochloride were administered subcutaneously to male rats. Measurement of GABA in the rat brains by the enzymatic method of Jakoby and Scott (1959) shows that morphine and naloxone had no significant effect on regional steady-state concentrations of GABA. The results were discussed in the context of the GABA role in pain and analgesia. 9 references. (Author abstract modified)

003085 Sharkawi, M.; Cianflone, D. Department of Pharmacology, Faculty of Medicine, University of Montreal, Montreal, P.Q., Canada **Disulfiram-induced hypothermia in the normal rat; its attenuation by pimozide.** Neuropharmacology (Oxford). 17(6):401-404, 1978.

Intraperitoneal injection of disulfiram, a dopamine-beta-hydroxylase inhibitor (DBHI), produced a dose dependent hypothermia in normal rats which was significantly reduced by pimozide, a selective blocker of dopamine receptors. Intraperitoneal injection of another DBHI, methimazole, also produced hypothermia in normal rats that was significantly reduced by pimozide. Since pimozide significantly reduced the hypothermia induced by the two DBHIs, it appears that the hypothermic response may involve activation of dopamine receptors. 12 references. (Author abstract modified)

003086 Sharma, J. N.; Sandrew, B. B.; Wang, S. C. Department of Pharmacology, Columbia University College of Physicians and Surgeons, New York, NY 10032 **CNS site of clonidine-induced hypotension: a microiontophoretic study of bulbar cardiovascular neurons.** Brain Research (Amsterdam). 151(1):127-133, 1978.

The effects of clonidine applied microiontophoretically to bulbar cardiovascular neurons which play a chief role in the regulation of blood pressure were investigated. To localize the central site and mechanism of clonidine-induced hypotension, the drug was applied by the technique of microiontophoresis to neurons of the bulbar cardiovascular center in decerebrate cats. The excitatory and inhibitory cardiovascular neurons (CVN) were identified by their response to an increase in the arterial blood pressure induced by intravenous injections of small doses of norepinephrine (NE). Clonidine had an inhibitory effect on the spontaneous firing rate of excitatory CVN but had no effect on the firing rate of noncardiovascular neuron (NCVN) recorded from the same area. It is concluded that clonidine produces its hypotensive responses by acting on alpha adrenergic receptors of bulbar CVN. 22 references. (Author abstract modified)

003087 Shenkman, L.; Traficante, L. J.; Rotrosen, J.; Gershon, S. Department of Medicine, New York University Medical center, 550 First Ave., New York, NY 10016 **Effects of lithium on the membrane-bound magnesiumdependent ATPase of mouse neuroblastoma cells.** Communications in Psychopharmacology. 2(1):65-72, 1978.

The effect of lithium on the membrane bound magnesium (Mg) dependent ATPase of an adrenergic clone of mouse neuroblastoma was examined. Growing the neuroblastoma cells in the presence of lithium (2.5mEQ/L) did not affect the activity, pH optimum or temperature sensitivity of the enzyme. In vitro addition of lithium to cell membrane preparations likewise did not alter enzyme activity. It is concluded that while lithium has been shown to affect several Mg dependent enzymes, it has no apparent effect on the Mg dependent ATPase of mouse neuroblastoma. 11 references. (Author abstract)

003088 Sheppard, H.; Burghardt, C. R.; Long, J. P. Department of Cell Biology, Roche Research Center, Hoffman-La Roche, Inc., Nutley, NJ **The effect of dihydroxy-2-aminotetralins (DATs) on dopamine and beta type adenylate cyclases.** Research Communications in Chemical Pathology and Pharmacology. 19(2):213-224, 1978.

The mode of action and relative potency of dihydroxy-2-aminotetralins (DATs) were evaluated for their abilities to alter the activities of the dopamine and beta type cyclases. Dopamine adenylate cyclase and beta adenylate cyclase, prepared from the adult male rat frontal cortex and rat erythrocytes, respectively, were assayed for cyclic AMP and measure for agonist activity. Of the various 2-aminotetralins, JOD-176 and M-8 were found to be potent beta agonists. With systems designed to detect dopamimetic activity in vivo, M-7, M-8 and ADTN were found to possess agonist activity. As agonists of the dopamine sensitive adenylate cyclase, ADTN was more active than some 5, 6-DATs. None of the compounds tested possessed antagonist activity. A new view was constructed which suggests that the nitrogens of the DAT compounds are positioned better than those of the model compounds with regard to their binding sites. 17 references. (Author abstract modified)

003089 Sheppard, Herbert; Brughardt, Charles R. Department of Cell Biology, Roche Research Center, Hoffmann-La Roche, Inc., Nutley, NJ 07110 **The dopamine-sensitive adenylate cyclase of the rate caudate nucleus -- 3. The effect of aporphines and protoberberines.** Biochemical Pharmacology (Oxford). 27(8):1113-1116, 1978.

A series of aporphines and protoberberines were tested for activity with the dopamine (DA) sensitive adenylate cyclase of the rat caudate nucleus and the beta sensitive adenylate cyclase of the rat erythrocyte. Loss of DA agonist but not antagonist activity of apomorphine was associated with the removal of meth-

ylation of the hydroxyls or the S-configuration. The effects of other alterations in structure were not as clear cut, and alterations in antagonist activity were not similar in the two enzyme systems. The protoberberines were fairly potent as inhibitors of the DA cyclase with little effects on the beta system. In most situations, the S-isomer was much more potent than the R-antipode. None of the compounds studied possessed beta-agonist activity. 17 references. (Author abstract)

003090 Siegel, S. Department of Psychology, McMaster University, Hamilton, Ontario L8S 4K1, Canada **The role of Pavlovian conditioning in morphine tolerance.** Psychopharmacology (Berlin). 58(2):10, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, studies of the role of Pavlovian conditioning in morphine tolerance were reported. Findings indicate that the display of tolerance is specific to the environment in which the drug has been previously administered. Established tolerance can be extinguished by repeated placebo sessions, and interpolating placebo sessions among drug sessions impedes the acquisition of tolerance. Experience with drug administration cues prior to their pairing with morphine also impedes the acquisition of tolerance. These data, together with evidence of the effects of tolerance on electroconvulsive shock, metabolic inhibitors, and pituitary vasopressin, indicate the importance of associative mechanisms in the acquisition of tolerance.

003091 Simler, S.; Gensburger, C.; Ciesielski, L.; Mandel P. Centre de Neurochimie du CNRS, Faculte de Medecine, ll, rue Humann, F-67085 Strasbourg Cedex, France **Time course of the increase in GABA level in different mice brain regions following N-dipropylacetate treatment.** Communications in Psychopharmacology. 2(2):123-130, 1978.

The time course of the increase in GABA level in different mice brain regions following n-dipropylacetate treatment was studied using male Swiss albino brain of 1 mice sacrificed, after interperitoneal administration of sodium n-dipropylacetate (a competitive inhibitor of GABA transaminase). The concentration of GABA increased in many areas with the highest GABA level increases observed in olfactory bulb, hypothalamus, substantia nigra, superior and inferior colliculus, and amygdala. The GABA level remained undamaged in the caudata nucleus and in the temporal cortex. The increase of GABA is not uniform in the different brain areas and is not a function of the initial GABA level. 30 references. (Author abstract modified)

003092 Simon, Eric J.; Hiller, Jacob M. Department of Medicine, New York University Medical Center, New York, NY 10016 **The opiate receptors.** Annual Review of Pharmacology and Toxicology. 18:371-394, 1978.

The most significant advances made in man's knowledge of opiate receptors since their discovery are reviewed. The receptor postulate and discovery of opiate binding sites, properties of these sites, regional distribution of opiate receptors, ontogeny of the opiate receptor, discovery of endogenous opiate-like peptides, conformational changes in opiate receptors, progress in solubilization and purification of opiate receptors, other types of binding material for opiates, biochemical events following opiate binding, studies in cell and tissue culture, and environmental effects on opiate receptors are discussed. Research on the mode of action of opiates received an enormous boost from the discovery of the long postulated opiate receptors and from the consequent discovery of endogenous opiate peptides, endorphins, which are natural ligands for opiate receptors. Although the field is moving at a rapid pace, much remains to be learned to promote a better understanding of the workings of the human and animal brain. 115 references.

003093 Skellern, Graham G.; Mahmoudian, Massoud. Drug Metabolism Research Unit, Department of Pharmaceutical Chemistry, University of Strathclyde, Glasgow, G1 1XW, Scotland **The uptake of (35S)methimazole by sheep thyroid slices in vitro.** Biochemical Pharmacology (Oxford) 27(5):685-691, 1978.

The uptake of (35S)methimazole by sheep thyroid slices was examined in the presence of iodide. The total uptake of (35S)methimazole was found to be the sum of a saturable process and a nonsaturable process. Diiodotyrosine (0.1mM) stimulated the saturable uptake of (35S)methimazole appreciably in the absence of iodide, while thyroid stimulating hormone inhibited uptake in the presence of iodide and had no effect in its absence. Propylthiouracil inhibited the saturable uptake of (35S)methimazole, while perchlorate had no effect. 26 references. (Author abstract modified)

003094 Sklenovsky, A.; Chmela, Z. Dept. of Pathophysiology, Dr. S. Allenak 3, 77515 Olomouc, Czechoslovakia **Changes in brain free fatty acids after painful peripheral stimulation (effect of prothiaden).** Activitas Nervosa Superior (Praha). 29(1):63-64, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the effect of prothiaden, a drug which inhibits brain phospholipase-A (PA) activity on changes in brain free fatty acids, nonesterified free fatty acids, (NEFA), following painful peripheral stimulation, is described. Shock applied to rats led to an increase of NEFA; the application of prothiaden decreased NEFA reaction to shock. Results confirm previous conclusions on the mechanism of action of neuropharmacological drugs influencing brain PA. 4 references.

003095 Slater, I. H.; Jones, G. T.; Moore, R. A. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Inhibition of REM sleep by fluoxetine, a specific inhibitor of serotonin uptake.** Neuropharmacology (Oxford). 17(6):383-389, 1978.

Fluoxetine, a specific inhibitor of serotonin (5-hydroxytryptamine, 5-HT) uptake, suppressed rapid eye movement (REM) sleep in cats. The onset of action was prompt and lasted a full 24 hours at oral doses of 2.5mg/kg. After 2 to 3 weeks of daily fluoxetine, the amount of REM sleep began to increase again. A small dose of fluoxetine added to a small dose of L-5-hydroxy tryptophan caused a significant decrease in REM sleep, whereas either treatment alone did not. Administered to cerveau isole cats, fluoxetine did not antagonize electroencephalogram desynchronization induced by the muscarinic stimulant arecoline, indicating the lack of a direct anticholinergic effect. REM sleep is suppressed by the accumulation of 5-HT or norepinephrine (NE) at synapses, suggesting that both 5-HT and NE can inhibit the cholinergic system involved in REM sleep. 16 references. (Author abstract modified)

003096 Somoza, E. Department of Investigation, "Ramon y Cajal" Centre, Madrid-34, Spain **Influence of neuroleptics on the binding of met-enkephalin, morphine and dihydromorphine to synaptosome-enriched fractions of rat brain.** Neuropharmacology (Oxford). 17(8):577-581, 1978.

The effects of haloperidol, chlorpromazine, and prochlorperazine on the binding of tritiated met-enkephalin to synaptosome enriched fractions of female Wistar rat brain were studied in the high affinity binding region. All three neuroleptics blocked the binding of met-enkephalin in a dose dependent fashion, with inhibition constants of 11.6, 39.5, and 29.5mcM for haloperidol, chlorpromazine, and prochlorperazine, respectively. Hill plots

suggested that the inhibitory mechanism involves negative allosteric effects between neuroleptic molecules. The effects of these neuroleptics on the binding of tritiated morphine and dihydromorphine were also studied. Results are discussed in relation to the possible involvement of endogenous opiates in the antipsychotic effect of neuroleptics. 22 references. (Author abstract modified)

003097 Soukup, Joseph F.; Friedel, Robert O.; Schanberg, Saul M. Department of Pharmacology, Duke University Medical Center, Durham, NC 27710 **Cholinergic stimulation of polyphosphoinositide metabolism in brain in vivo.** Biochemical Pharmacology (Oxford). 27(8):1239-1243, 1978.

The effect of carbamylcholine (CARB) on phosphate and inositol incorporation into phosphoinositides (PPI) in regions of rat brain were examined in vivo, using intracisternal administration of radioisotopes and drugs and microwave irradiation fixation. PPI incorporation of phosphate and inositol increased 50-100% in response to CARB within 5 minutes of drug and label administration. These responses were greater in the cerebral cortex and brainstem/midbrain regions than in the cerebellum and were blocked by intraperitoneal pretreatment with atropine sulfate. Increases in substrate PPI were not accompanied by detectable increases in PPI concentration, suggesting that PPI turnover was stimulated. CARB also increased isotope incorporation into PPI precursors phosphatidic acid (PA) and monophosphoinoside (MPI), and there was no evidence to suggest that the CARB effects on PA and MPI and those on PPI represent different phenomena. Results suggest that PPI, like PA and MPI, are associated with membrane events that result from neurotransmitter activation of cholinergic receptors in brain. 40 references. (Author abstract)

003098 Steranka, Larry R.; Sanders-Bush, Elaine. Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232 **Long-term effects of continuous exposure to p-chloroamphetamine on central serotonergic mechanisms in mice.** Biochemical Pharmacology (Oxford). 27(16):2033-2037, 1978.

The intraperitoneal administration of 45mg/kg p-chloroamphetamine (PCA) in male albino mice produced decreases in brain levels of 5-hydroxytryptamine (5-HT), 5-hydroxyindoleacetic acid, and tryptophan hydroxylase activity shortly after injection, but substantial recovery was evident within 2 weeks of PCA administration. Regional analyses indicate that the hippocampus and remaining telencephalon were most sensititive to the PCA-induced decrease in 5-HT levels, but complete recovery was observed within 1 month of PCA treatment even in these relatively sensitive areas. Continuous release of PCA from subcutaneously implanted minipumps for a period of 3 days produced decrease in brain levels of 5-HT that lasted for at least 4 weeks. Results indicate that the insensitivity of mice to the neurotoxic effects of PCA is related to its relatively short half-life in this species. 20 references. (Author abstract modified)

003099 Stolzki; Bernd; Kaiser, Hartmut O.; Mehl, Ehrenfried L. Division of Neurochemistry, Max-Planck-Institut for Psychiatrie Kraepelinstr. 2, 8 Munchen 40, Germany **Heterogeneity of LSD-displacing factors and multiple types of high affinity LSD-binding sites.** Life Sciences (Oxford). 23(6):593-598, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Atagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, studies on the specificity of association of lysergic acid diethylamide (LSD) displacing factors with specific organs from the Sprague-Dawley rat are reported. Heterogeneity of the high affinity LSD binding sites was confirmed by displacement studies with 2-bromo()-LSD and with apamin, a peptide neurotoxin. In line with the concept of multiple binding sites, a number of fractions of putative endogenous ligands could be separated from rat brain extract. The LSD displacing beta-fraction was not detectable in tissues lacking high affinity LSD-binding sites. igh affinity dopamine and serotonin binding was differentially affected by the beta-fraction. 13 references. (Author abstract modified)

003100 Stone, Eric A. Millhauser Laboratories of the Department of Psychiatry, New York University School of Medicine, 550 First Avenue, New York, NY 10016 **Effect of stress on norepinephrine-stimulated cyclic AMP formation in brain slices.** Pharmacology Biochemistry and Behavior. 8(5):583-591, 1978.

The effect of stressful procedures that increase brain norepinephrine (NE) release on the responsiveness of central NE receptors was examined by measuring the catecholamine-induced accumulation of cyclic adenosine monophosphate (AMP) in rat hypothalamic and cerebral cortical slices. No conclusive evidence of subsensitivity was found after wither acute or chronic electric footshock or continuous restraint. Failure to find a significant reduction in cyclic AMP accumulation after stress may be attributable to several methodological problems, including the inhibition of phosphodiesterase activity with isobutylmethylxanthine, a low initial responsiveness to NE, and the use of exogenous NE as a test agent. 38 references. (Author abstract modified)

003101 Stone, T. W.; Taylor, D. A. Department of Physiology, St. George's Hospital Medical School, University of London, Cranmer Terrace, London SW17 ORE, England **Interactions between guanine derivatives and norepinephrine on neurones of the mammalian cerebral cortex.** Brain Research (Amsterdam). 155(1):187-191, 1978.

Interactions of guanines and norepinephrine on central neurons were examined in rats by applying the compounds to single cells by microiontophoresis and by measuring the amplitude and duration of each norepinephrine response. Norepinephrine responses were reduced on 15 neurons and were enhanced on 22; the responses of 31 neurons were unaffected by the guanines. The most commonly observed interaction between 5'-guanosine monophosphate (5'-GMP) or guanosine triphosphate (GTP) and norepinephrine was enhancement of the amine responses which seemed to be an enhancement of norepinephrine by the nucleotide and not a mutual effect. The finding that several neurons did not respond at all to norepinephrine until 5'-GMP or GTP was applied raises the possibility that neuronal responses to nnorepinephrine could be modulated by the release of nucleotide from other neurons. The fact that low concentrations of guanine nucleotides can inhibit adenylate cyclase could underlie an observation that some neurons experienced a reduction of norepinephrine responses. 22 references.

003102 Stramentinoli, Giorgio; Baldessarini, Ross J. Dept. of Biochemistry, Bio Research Co., 20060 Liscate, Milan, Italy **Lack of enhancement of dimethyltryptamine formation in rat brain and rabbit lung in vivo by methionine or S-adenosylmethionine.** Journal of Neurochemistry (Oxford). 31(4):1015-1020, 1978.

The possible conversion of tryptamine to N-methyltryptamine (NMT) or n,n-dimethyltryptamine (DMT) in rat brain was studied and the indoleamine transmethylation pathway of the rabbit lung in vivo following large doses of methionine or S-adenosyl-L-methionine (SAMe) was evaluated. In vivo conversion of intracisternally administered (14C)tryptamine to (14C)DMT in rat brian, even in the presence of an excess of substrate and methyl donor was found to be insignificant, although enzymatically synthesized (14C)DMT was recovered readily after intracranial injection. In rabbit lung, the apparent Km for SAMe (29mcM) with indolethylamine-N-methyltransferase was found to be close

to endogenous levels of SAMe (34mcM) that are not likely to saturate the enzyme normally. Large doses of L-methionine or SAMe failed to increase the in vivo conversion of (14C)NMT to (14C)DMT in this tissue. The production of (14C)DMT was instead markedly inhibited by this treatment, possibly due to an effect of S-adeno-sylhomocysteine. These results fail to support the hypothesis that psychotropic effects of methionine or SAMe are due to increased accumulations of pharmacologically active methylated indoleamines. 26 references. (Author abstract modified)

003103 Sugrue, Michael F.; Mireyless, Stewart E. Centre de Recherche Merrell International, 16 rue d'Ankara, F-67084 Strasbourg, France **Effects of mazindol on rat brain synaptosomal monoamine uptake.** Biochemical Pharmacology (Oxford). 27(14):1843-1847, 1978.

The effects of mazindol, d-amphetamine, dl-fenfluramine, chlorimipramine, and desipramine on the uptake of tritiated norepinephrine (3H-NE) and 5-hydroxytryptamine (3H-5-HT) by hypothalamic synaptosomes and the uptake of tritiated dopamine (3H-DA) by striatal synaptosomes were compared in male Wistar rats, both in vivo and in vitro. Mazindol was a potent inhibitor of 3H-NE and 3H-DA uptake in vitro (about 0.5times as potent as desipramine and d-amphetamine, respectively). Mazindol, fenfluramine, and desipramine showed comparable abilities in blocking the in vitro uptake of 3H-5-HT, and all three drugs were appreciably less potent than chlorimipramine. Following 1 hour pretreatment, d-amphetamine was the most potent of the five drugs at inhibiting synaptosomal 3H-NE and 3H-DA uptake. Mazindol was about 2.5time more potent than desipramine at blocking 3H-NE uptake. In contrast to the other drugs, pretreatment with large doses of mazindol had essentially no effect on hypothalamic synaptosomal 3H-5-HT uptake. These results indicate that mazindol is a selective inhibitor of rat brain catecholamine uptake. 29 references. (Author abstract modified)

003104 Suzuki, O.; Katsumata, Y.; Oya, Masakazu; Hari, V. M.; Klapfenberger, R., Wagner, H. Division of Neurotoxicology, Department of Legal Medicine, Nagoya University School of Medicine, Nagoya 466, Japan **Inhibition of monoamine oxidase by isogentisin and its 3-0-glucoside.** Biochemical Pharmacology (Oxford). 27(16):2075-2078, 1978.

The effects of isogentisin (1,3-dihydroxy-7-methoxyxanthone) and its 3-0-glucoside on monoamine oxidase (MAO) activity in homogenates of male Sprague-Dawley rat brain were examined. With kynuramine as substrate, both compounds were potent inhibitors of rat brain mitochondrial MAO in vitro. The inhibitory potency of isogentisin was comparable to that of pargyline and harmaline, whereas the 3-0-glucoside was much less effective. Inhibition of rat brain MAO by both compounds was fully competitive. 10 references.

003105 Swanson, L. W.; Connelly, M. A.; Hartman, B. K. Department of Anatomy and Neurobiology, and Psychiatry, Washington University School of Medicine, St. Louis, MO 63110 **Further studies on the fine structure of the adrenergic innervation of the hypothalamus.** Brain Research (Amsterdam). 151(1):165-174, 1978.

The posterolateral two thirds of the paraventricular nucleus of the hypothalamus was examined in an effort to better understand the fine structural characteristics of central aminergic terminals. A dose of .05-3.0mg 5-hydroxydopamine (5-OHDA) was injected into the lateral ventricle of superior/cervicle ganglionectomized rats 30 minutes before perfusion with a buffered mixture of aldehydes. Frozen sections were examined using both light and electron microscopes. Distinct synaptic membranes specializations, most often asymmetrical in appearance, were seen in 19% of labeled profiles. Examples of clear microvesicle containing varicosities were found in the paraventricular nucleus of animals not injected with 5-OHDA. It is suggested that monoaminergic varicosities can be seen in normal material, and that the size of the vesicles within them in the experimental material is not an artificial result of loading with 5-OHDA. Furthermore, findings suggest quite separate ways in which the adrenergic system may influence the function of the paraventricular nucleus. 38 references.

003106 Tabakoff, B.; Hoffman, P. L.; Ritzmann, R. F. Department of Physiology and Biophysics, University of Illinois at the Medical Center, P.O. Box 6998, Chicago, IL 60680 **Dopamine receptor function after chronic ingestion of ethanol.** Life Sciences (Oxford). 23(6):643-647, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, changes in dopamine receptors after chronic ethanol ingestion in C57B1/6 mice are reported. Animals withdrawn from an ethanol containing diet were much less sensitive to the hypothermic and locomotion inducing effects of dopamine receptor agonists. The ethanol withdrawn animals also failed to show the neuroleptic-induced stimulation of DOPA synthesis seen in control animals. The subsensitivity of the ethanol withdrawn animals to the effects of neuroleptics and dopamine receptor agonists showed similar time course: in both measures, normal drug effects were apparent approximately 3 days after withdrawal. Preliminary studies suggest that the aberration in dopamine receptor function may be mediated by changes in receptor/ effector coupling due to adaptive changes in neuronal membranes in response to the chronic presence of ethanol. 16 references. (Author abstract modified)

003107 Tabakoff, Boris; Hoffman, Paula L. Department of Physiology and Biophysics, University of Illinois at the Medical Center, Chicago, IL 60612 **Alterations in receptors controlling dopamine synthesis after chronic ethanol ingestion.** Journal of Neurochemistry (Oxford). 31(5):1223-1229, 1978.

The influence of chronic and acute ethanol treatment and withdrawal on regulation of dopamine (DA) synthesis in striatal and mesolimbic areas of C57B1/6 mouse brain was examined. Eight hours after a single (3g/kg) dose of ethanol, dihydroxyphenylalanine (DOPA) synthesis was increased, and pimozide stimulated DOPA synthesis to the same degree in ethanol-treated and control animals. Eight hours after withdrawal from chronic ethanol treatment, however, endogenous DA synthesis was the same in ethanol-withdrawn and control animals, but the stimulation of DA synthesis produced by low doses of pimozide or haloperidol was significantly less in the ethanol-withdrawn animals. This effect was even more apparent 24 hours after withdrawal, but by 3 days after withdrawal the decreased response of ethanol-withdrawn animals to the administration of DA receptor blockers was no longer significant. At all times, high doeses of pimozide or haloperidol stimulated DOPA synthesis equally in control and ethanol-withdrawn animals. It is concluded that chronic ethanol treatment and withdrawal may alter the coupling between DA receptors that regulate DA synthesis and tyrosine hydroxylase. 37 references. (Author abstract modified)

003108 Tachiki, K. H.; Takagi, A.; Tateishi, T.; Kido, A.; Nishiwaki, K.; Nakamura, E.; Nagayama, H.; Takahashi, R. Neurochemistry Laboratories, Veterans Administration Hospital, Sepulveda, CA **Animal model of depression: III. Mechanism of action of tetrabenazine.** Biological Psychiatry. 13(4):429-443, 1978.

The biochemical mechanism whereby tetrabenazine (TBZ) produces a sedative effect on the locomotor activity of rats was investigated. Rats injected with L-5-hydroxytryptophan (L-5-HTP, 30m/kg), the immediate precursor of 5-hydroxytryptamine (5-HT), showed the characteristic bison appearance, ptosis, and catalepsy normally observed after injecting TBZ (30mg/kg). The treatment of rats with low doses of L-5-HTP (9mg/kg) plus TBZ (2mg/kg) significantly decreased locomotor activity, whereas low doses of either one of these drugs given alone had no significant effect on locomotor activity. The level of 5-hydroxyindoleacetic acid (5-HIAA) was elevated in the brain of rats sacrified 3 hr after treatment with low doses of L-5-HTP (9mg/kg) plus TBZ (2mg/kg). No significant changes in the levels of 5-HIAA were observed in rats treated with low doses of either L-5-HTP or TBZ alone. Treatment of rats with p-chlorophenylalanine to inhibit the synthesis of 5-HT had an inhibitory effect on the duration of sedation following an injection of TBZ (30mg/kg). The results of the biochemical and pharmacological studies as reflected by changes in locomotor activity are interpreted to indicate that the sedative action of TBZ was due to an excess of functional 5-HT. 34 references. (Author abstract)

003109 Takano, K.; Student, J. G. Physiologisches Institut, Lehrstuhl II, Universitat Gottingen, Humboldtallee 7, D-3400 Gottingen, Germany **Erfect of diazepam on the gamma motor system indicated by the responses of the muscle spindle of the triceps surae muscle of the decerebrate cat to the muscle stretch.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 302(1):91-101, 1978.

The effect of diazepam given intravenously on the discharge frequencies of group Ia afferent fibers from muscle spindles in the belly of the triceps surae muscle was studied in 37 intercollicularly decerebrate cats. Diazepam depressed both the dynamic and the static gamma motor responses. When gamma motor fibers were selectively blocked by procaine a parallel shift of the tension/extension curve was observed. While differences in the effect of diazepam on the dynamic and static gamma system could not be found, it is concluded that directly after the injection of diazepam the gamma motor activity was completely abolished at a dose as low as 0.1mg/kg, whereas the alpha motor system was only partly depressed even at higher doses. 42 references. (Author abstract modified)

003110 Tessel, Richard E.; Kennedy, L. Elaine; Burgess, Susan K.; Borchardt, Ronald T. Department of Pharmacology, University of Kansas, Lawrence, KS 66044 **Epinephrine in rat hypothalamus: antagonism by desipramine of 6- hydroxydopamine-induced depletion.** Brain Research. 153(3):615-617, 1978.

The effects of intraventricular 6-hydroxydopamine (6-OHDA) on both rat hypothalamic catecholamine content and phenylethanolamine N-methyltransferase (PNMT) activity were studied. In rats, intraventricular 6-OHDA treatment resulted in 81% and 56% depletions of hypothalamic norepinephrine and epinephrine, respectively; dopamine content was not significantly altered. Pretreatment with desipramine reduced the norepinephrine depletion to 34% and abolished the 6-OHDA-induced epinephrine depletion. PNMT activity was not significantly altered by 6-OHDA. The results suggest that PNMT activity per se is not an adequate index of epinephrine neuronal integrity. 15 references.

003111 Tessel, Richard E.; Burgess, Susan K.; Rutledge, Charles O. Department of Pharmacology and Toxicology, School of Pharmacy, University of Kansas, Lawrence, KS 66045 **Release of endogenous catecholamines from isolated rat brain tissue by fenfluramine and N-ethylamphetamine -- effects of pargyline.** Biochemical Pharmacology (Oxford). 27(12):1631-1636, 1978.

The influence of the monoamine oxidase inhibitor, pargyline, on the fenfluramine- and N-ethylamphetamine-induced release of endogenous norepinephrine (NE) from chopped cerebral cortex and of endogenous dopamine (DA) from chopped corpus striatum was investigated in male Sprague-Dawley rats. Fenfluramine-induced catecholamine release was associated with a decrease in the total content of cortical NE and striatal DA, whereas N-ethylamphetamine decreased only total striatal DA content. Pretreatment with pargyline (100mg/kg) doubled the total cortical NE content and had no effect on striatal DA content. Pargyline pretreatment also resulted in a marked potentiation of the amounts of both catecholamines released by each drug and in antagonism of the drug-induced reductions in catecholamine content. Results suggest that pargyline potentiates the behavioral effects of fenfluramine and N-ethylamphetamine by increasing the pool of NE available for release by these drugs and by inhibiting the deamination of the released catecholamines by monoamine oxidase. 23 references. (Author abstract modified)

003112 Thal, L. J.; Makman, M. H.; Ahn, H. S.; Mishra, R. K.; Horowitz, S. G.; Dvorkin, B.; Katzman, R. Department of Neurology, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461 **3H-spiroperidol binding and dopamine-stimulated adenylate cyclase: evidence for multiple classes of receptors in primate brain regions.** Life Sciences (Oxford). 23(6):629-634, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, evidence for multiple classes of dopamine receptors in Cebus and rhesus monkey brain regions is discussed. Studies of displacement by agonist and antagonist drugs of 3H-spiroperidol binding revealed one type of receptor in caudate nucleus and a second type of receptor in frontal and anterior limbic cortex. Compared with caudate, cortical regions were more sensitive to clozapine and loxapine, equally sensitive to fluphenazine and less sensitive to haloperidol. Parallel studies using dopamine stimulated adenylate cyclase demonstrated three types of receptors, one in caudate, a second in frontal cortex, and a third in anterior limbic cortex. In each region studied, relative sensitivities to drugs using these two methods differed, suggesting that a relatively small portion of 3H-spiroperidol receptors are coupled to adenylate cyclase in these regions. 18 references. (Author abstract modified)

003113 Thal, Leon; Creese, Ian; Snyder, Solomon H. Department of Neurology, Albert Einstein College of Medicine, Bronx, NY 10461 **3H-apomorphine interactions with dopamine receptors in calf brain.** European Journal of Pharmacology (Amsterdam). 49(3):295-299, 1978.

The binding of 3H-apomorphine to dopamine receptors in various regions of calf brain was characterized. 3H-apomorphine binding to membranes from areas of the corpus striatum and limbic system was saturable and showed a drug specificity, indicating that it labels dopamine receptors. In terms of drug specificity, log/logit displacement curve slopes, and number of binding sites, 3H-apomorphine interacted with receptors in a manner more like 3H-dopamine than 3H-haloperidol. These properties of 3H-apomorphine binding are those of an apparently pure agonist, in contrast to the partial agonist effects of apomorphine on dopamine. 11 references. (Author abstract modified)

003114 Tilstone, W. J.; Reavey, P. C. Forensic Science Unit, Department of Pharmaceutical Chemistry, University of Strathclyde, Glasgow, Scotland **Ethanol and disposition of amylobarbi-**

tone: effect of dose and significance as a mechanism for increased toxicity. Journal of Pharmacy and Pharmacology (London). 30(5):319-320, 1978.

The effects of hypnotic and nonhypnotic doses of ethanol on the effects, distribution, and elimination of amylobarbitone were studied in adult male Wistar rats. Drugs were administered intraperitoneally, and plasma disappearance of amylobarbitone was measured by collecting blood from rats decapitated at various intervals between and 20 and 300 minutes after injection. In all experiments, administration of ethanol increased the duration of loss of righting reflex but did not effect the minimum effective dose of amylobarbitone. Prolongation of amylobaritone half-life by a hypnotic dose of ethanol was due partly to impaired amylobarbitone metabolism. The results indicate that the fractional elimination of amylobarbitone is reduced by concomitant administration of ethanol, the effect of hypnotic doses thereby being prolonged, but only at high doses of ethanol do the results support the in vitro observations of altered barbiturate metabolism. The interaction occurs with doses of ethanol which are well below the measured minimum hypnotic dose of ethanol given by itself. 7 references.

003115 Tilstone, William J.; Reavey, Philip C. Forensic Science Unit, Department of Pharmaceutical Chemistry, University of Strathclyde, Glasgow, G1 1XW, Scotland **Interaction of ethanol with amylobarbitone, phenobarbitone and methaqualone.** Research Communications in Chemical Pathology and Pharmacology. 19(2):233-242, 1978.

The synergistic action between ethanol and amylobarbitone, phenobarbitone, and methaqualone was examined. Simple pharmacokinetic models were used for logging dose response curves and plasma concentration time curves in male rats for the three drugs alone or when ethanol was given concurrently. Results indicate that ethanol increased the duration of hypnosis for all the hypnotic drugs, but the mechanism of action was different for each. A subhypnotic dose of ethanol increased the volume of distribution of amylobarbitone and the consequent reduction in fractional elimination prolonged the half-life of the hypnotic. The distribution and elimination of methaqualone was not affected by ethanol, but there was a sensitization of the target organ, shown by a reduced minimum effective dose. The minimum effective dose of phenobarbitone was also reduced by ethanol, but in addition, the rate fof elimination of phenobarbitone was increased after the period of hypnosis. Mechanisms of interaction between ethanol and the three hypnotic drugs are discussed. 15 references. (Author abstract)

003116 Tissari, H. A.; Porceddu, M. L.; Argiolas, A.; Di Chiara, G.; Gessa, G. L. Department of Pharmacology, University of Helsinki, Finland **Dopamine-synthesis and tyrosine-hydroxilase are regulated by independent DA-receptor mediated mechanisms.** Life Sciences (Oxford). 23(6):653-658, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, a study of dopaminergic feedback was described. Intrastriatal injection of kainic acid prevented the increase in tyrosine hydroxylase (TH) cofactor affinity but not the in vivo stimulation of dopamine (DA) synthesis produced by haloperidol in rats. Destruction of corticostriatal input by decortication did not prevent the effect of haloperidol or apomorphine on striatal DA metabolism. Results suggest that postsynaptic DA receptors control stable conformational changes of the TH molecule, while presynaptic DA receptors control DA synthesis. No evidence was obtained to support the suggestion that presynaptic DA receptors located on corticostriatal axons play a major role in the control of DA metabolism in vivo. 22 references. (Author abstract modified)

003117 Titeler, Milt; Tedesco, Joseph L.; Seeman, Philip. Department of Pharmacology, Faculty of Medicine, University of Toronto, Toronto, Canada M5S 1A8 **Selective labeling of presynaptic receptors by 3H-dopamine, 3H-apomorphine and 3H-clonidine; labeling of post-synaptic sites by 3H-neuroleptics.** Life Sciences (Oxford). 23(6):587-591, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the effects of nanomolar (nM) concentrations of dopaminergic agonists and antagonists on the binding of tritiated dopamine, spiperone, apomorphine, and dihydroergocryptine to calf caudate tissue are reported. Dopamine agonists (apomorphine, N-propyl-norapomorphine, and bromocryptine) inhibited 3H-spiperone binding, but not 3H-dopamine binding, in direct correlation to their clinical potencies. Dopamine agonists inhibited 3H-apomorphine binding at concentrations indentical to those causing presynaptic cardioinhibition. The median inhibitory concentration (IC50) values for 3H-clonidine binding, but not for 3H-dihydroergocryptine binding, correlated with the presynaptic IC50 values for affecting noradrenaline release. Results are compatible with the hypothesis that nM concentrations of 3H-dopamine, 3H-apomorphine, and 3H-clonidine bind to presynaptic sites, while nM concentrations of 3H-neuroleptics and 3H-dihydroergocryptine bind to presynaptic sites. 30 references. (Author abstract modified)

003118 U'Prichard, David C.; Greenberg, David A.; Sheehan, Peter P.; Snyder, Solomon J. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Tricyclic antidepressants: therapeutic properties and affinity for alpha-noradrenergic receptor binding sites in the brain.** Science. 199(4325):197-198, 1978.

The relative potencies for seven tricyclic antidepressants in competing for the binding of 3H-labeled WB-4101 to alpha-noradrenergic receptor sites in rat brain membranes were investigated. The tertiary amines doxepin, amitriptyline, chlorimipramine, and imipramine, and the secondary amines nortriptyline, desipramine, and protriptyline were tested. It was found that the affinities of the drugs for alpha-noradrenergic receptor sites in the brain correlate well with the capacity of the drugs to relieve psychomotor agitation and induce sedation and hypotension. These affinities were also found to correlate inversely with tendencies to elicit psychomotor activation. 25 references. (Author abstract modified)

003119 U'Prichard, David C.; Snyder, Solomon H. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **3H-catecholamine binding to alpha-receptors in rat brain: enhancement by reserpine.** European Journal of Pharmacology (Amsterdam). 51(2):145-155, 1978.

Binding studies showed that both ()-3H-epinephrine and (-)-3H-norepinephrine bind to male Sprague-Dawley rat cortex membranes in a saturable manner with dissociation constants of 16.7and 27nM, respectively. The maximum number of 3H-catecholamine binding sites (10-12pmoles/g tissue) and the pharmacological characteristics of ()-3H-epinephrine binding indicated that the catechlolamines label the same alpha-noradrenergic receptor in the rats as does 3H-clonidine. At 25 degrees, ()-3H-epinephrine binding associated rapidly to equilibrium and dissociated in a biphasic manner. The affinities of alpha-agonists at the 3H-catecholamine binding site were two to four weaker in the rat than in the calf cortex under the same conditions. Ergot alkaloids and phenoxybenzamine had similar affinities in the two tissues, whereas phentolamine and WB-4101 were 8-10 times weaker in the rat. Reserpine (0.25mg/kg/day for 3 weeks) caused 25% and 46% increases in the numbers of ()-3H-epineph-

rine and 3H-WB-4101 alpha-receptor binding sites, respectively, and a 51% increase in the number of 3H-dihydroalprenolol beta-receptor sites in rat forebrain. Reserpine pretreatment did not alter the affinities of either alpha-receptor or beta-receptor 3H-ligands. 26 references. (Author abstract modified)

003120 Urano, Akihisa; Sekijima, Naoko. Department of Zoology, NJ-15, University of Washington, Seattle, WA 98195 **The decrease of monoamine oxidase activity following the intraocular injection of colchicine in the superior colliculus of the rat.** Brain Research (Amsterdam). 159(1):243-246, 1978.

The effect of intraocular injection of colchicine on monoamine oxidase (MAO) activity in the superficial gray layer (SGL) of the superior colliculus was investigated in male Wistar rats, using microspectrophotometry. Unilateral injections of colchicine resulted in a decrease in MAO activity in the SGL of the superior colliculus contralateral to the injected eye; a dose of 10mcg colchicine resulted in a 5% decrease in MAO activity, and a 100mcg dose resulted in a 12% decrease. The decrease in MAO activity in the SGL following intraocular colchicine injection is most plausibly explained by colchicine inhibition of the anterograde transport of MAO in the optic nerve fibers from the retinal ganglion cells to their terminals in the superior colliculus. 18 references.

003121 Van Calker, D.; Muller, M.; Hamprecht, B. Max-Planck-Institut fur Biochemie, 8033 Martinsried, Germany **Adrenergic alpha- and beta-receptors expressed by the same cell type in primary culture of perinatal mouse brain.** Journal of Neurochemistry (Oxford). 30(4):713-718, 1978.

Both the beta-adrenergic agonist isoproterenol and the alpha and beta-adrenergic agonist norepinephrine (NA) elevated the intracellular concentration of cyclic adenosine monophosphate (AMP) in cultures of dissociated perinatal mouse brain. This elevation was blocked by a beta-adrenergic antagonist but not by an alpha-adrenergic antagonist. The maximal level of cyclic AMP reached in the presence of isoproterenol was markedly higher than that found after exposure to NA. However, if NA was used along with an alpha-adrenergic antagonist, cyclic AMP levels as high as those after isoproterenol were found. Agonists with alpha-adrenergic activity including NA decreased the response to isoproterenol, and this decrease was blocked by alpha-adrenergic antagonists. It is concluded that the increase in the level of cyclic AMP following beta-adrenergic agonists is due to beta-receptor mediated stimulation of adenylate cyclase, while the inhibition of this effect by alpha-adrenergic agonists is mediated by adrenergic alpha-receptors. The alpha-adrenergic and beta-adrenergic receptors are likely to be located on the same cells, probably the most abundant putative glial precursor cells. 36 references. (Author abstract modified)

003122 van den Berg, Adriaan P.; Noordhoek, Jan; Savenije-Chapel, E. Maria; Koopman-Kool, Elisabeth. Department of Pharmacology, Erasmus University, Rotterdam, Netherlands **The development of sex differences in the demethylation of ethylmorphine and in its interaction with components of the hepatic microsomal cytochrome P450 system in mice.** Biochemical Pharmacology (Oxford) 27(5):627-633, 1978.

The development of sex differences in ethylmorphine N-demethylation and several components of the reaction chain were studied in hepatic microsomes from mice of the CPB-SE strain between 3 and 11 weeks of age. Sex-specific changes were observed in demethylation rate, type 1 spectral interaction, cytochrome P450 content, and ethylmorphine-induced stimulation of reduced nicotinamide adenine dinucleotide phosphate/cytochrome P450 reductase activity; these changes occurred mainly between weeks 3 and 7 and were observed only in females, indicating that the cytochrome P450 system is repressed by androgen during sexual maturation. The kinetic constants of demethylation developed differently from ethylmorphine binding constants. Changes in demethylase were mainly restricted to Km (Michaelis-Menten constant), while changes in type 1 binding only involved the maximum spectral change. Reduction of cytochrome P450 substrate complex does not appear to be rate limiting in ethylmorphine binding. It is suggested that immature mice possess a low basal level of ethylmorphine binding bype 1 sites, which is elevated selectively in females during sexual maturation. 55 references. (Author abstract modified)

003123 Vargiu, Lidia; Stefanini, E.; Musinu, C.; Saba, G. Institute of Pharmacology, University of Cagliari, I-09100 Cagliari, Italy **Possible role of brain serotonin in the central effects of ketamine.** Neuropharmacology (Oxford). 17(6);405-408, 1978.

Ketamine increased turnover of serotonin (5-hydroxytryptamine, 5-HT) in the rat brain. The effect persisted for several hours after the anesthetic effect of ketamine had terminated. Pretreatment with p-chlorophenylalanine, an inhibitor of 5-HT synthesis, or with methergoline, a 5-HT receptor blocker, potentiated the anesthetic and analgesic effect of ketamine. 22 references. (Author abstract)

003124 Viala, Denise; Vidal, Catherine. Laboratoire de Neurophysiologie Comparee, Universite Pierre et Marie Curie, F-75230 Paris, Cedex 05, France **Evidence for distinct spinal locomotion generators supplying respectively fore- and hindlimbs in the rabbit.** Brain Research (Amsterdam). 155(1):182-186, 1978.

The locomotor capabilities of the isolated cervicothoracic cord were compared with those of the entire spinal cord in curarized rabbit preparations injected with nialamide and DOPA, and data about intergirdle coordination in fictive locomotion is presented. Results indicate that the cervical and lumbosacral spinal cord have distinct locomotor pattern generators which can be released in the curarized preparation after an injection of DOPA. The more labile oscillators are the forelimb locomotion generators. Since the same rate of locomotor burst was recorded in fore and hindlimbs prior to spinal transection at Th12 level, it is maintained that the posterior generators have imposed their rhythm upon the anterior generators by a driving process. Thus, there appears to be more than one simple autonomous generator in the forelimb activation since the forelimb generator is driven by the handlimb generator. The results may provide additional information that ascending propriospinal pathways are not only activated by primary afferents, but can also make direct links between hind and forelimb generators themselves. 22 references.

003125 Vijayalakshmi, Venkataraman; Lele, Jayashree V.; Daginawala, Hatim F. Department of Biochemistry, Nagpur University, Nagpur, India **Effect of reserpine on the monoamine oxidase (MAO) activity in rat liver and brain.** Biochemical Pharmacology. 27(15):1985-1986, 1978.

A single injection of reserpine (0.2mg/100g) produced an increase in the activity of monoamine oxidase (MAO) in both the liver and brain of Norwegian rats. The increase in MAO activity was observed using either serotonin or tyramine as substrate. The maximum increase MAO activity was seen 72 hours after injection in liver, with both tyramine and serotonin as substrates, and in brain with serotonin as substrate. With tyramine as substrate, the maximum enzyme activity in brain was observe 96 hours after reserpine. In all cases, the MAO activity returned to normal by 120 hours. Results suggest that depletion of serotonin and tyramine can be accounted for by an increase in MAO activity. 10 references. (Author abstract modified)

003126 Vijayan, E.; McCann, S. M. Department of Physiology, University of Texas Health Science Center at Dallas, Dallas, TX 75235 **The effects of intraventricular injection of gamma-aminobuyric acid (GABA) on prolactin and gonadotropin release in conscious female rats.** Brain Research (Amsterdam). 155(1):35-43, 1978.

Various doses of GABA or 0.9% NaCl in a volume of 2 mcl were injected into the third ventricle in conscious, free moving, Sprague-Dawley rats and the effect on luteinizing hormone and prolactin release was evaluated by measurements of plasma levels by immunoassay. Ss were both ovariectomized and ovariectomized estrogen progesterone pretreated rats. The effects of both these doses and doses of bicuculline, the GABA blocker, are reported and discussed. The results are interpreted to mean that GABA can stimulate release of luteinizing releasing hormone from the hypothalamus and that at low doses it can inhibit prolactin release, probably by a hypothalamic action. This effect is reversed at high doese to produce stimulation of prolactin release which is also probably mediated by the hypothalamus. 21 references. (Author abstract modified)

003127 Villa, R. F.; Strada, P.; Dagani, F.; Benzi, G. Department of Pharmacology, Uniersity of Pavia, Piazza Botta, 11, I-27100 Pavia, Italy **Magnification of some enzymatic activities of brain cortex subfractions.** Biochemical Pharmacology (Oxford). 27(18):2278-2280, 1978.

The effect of the catecholamine-like agent bamethan (1-p-hydroxyphenyl-2-butylamino-ethanol) on enzymatic activities in mitochondrial and synaptosomal subfractions of female Sprague-Dawley rat cortex were examined. All the enzymatic activity tested (lactate dehydrogenase, citrate synthase, malate dehydrogenase, nicotinamide adenine cytochrome c reductase, and cytochrome oxidase) showed significantly higher values in the pure mitochondria of rats treated with bamethan in vivo. Treatment with bamethan also magnified enzymatic activities, with the exception of citrate synthase, in the synaptosomal fraction. 14 references.

003128 Vincent, J. P.; Cavey, D.; Kamenka, J. M.; Geneste, P.; Lazdunski, M. Centre de Biochimie, Faculte des Sciences, Parc Valrose, 06034 Nice, France **Interaction of phencyclidines with the muscarinic and opiate receptors in the central nervous system.** Brain Research (Amsterdam). 152(1):176-182, 1978.

A series of 12 different molecules in the phencyclidine series were assayed for their ability to interfere with the binding of (3H)strychnine to the glycine receptor, (3H)glutamate with the glutamate receptor, (3H)dopamine with the dopamine receptor, (3H)dihydroalprenolol with the beta-adrenergic receptor, (3H)dihydromorphine with the opiate receptor, (3H)gamma-aminobutyric acide with the GABA receptor, (3H)serotonin with the serotonin receptor, and (3H)quinuclidinyl benzilate with the muscarinic receptor. Phencyclidines interfered only with the association of (3H)quinuclidinyl benzilate with the muscarinic receptor and the association of (3H)dihydromorphine with the opiate receptor. The properties of these interactions with the opiate and muscarinic receptors are described. 26 references.

003129 vom Saal, Frederick S. Institute of Reproductive Biology, Department of Zoology, University of Texas, Austin, TX 78712 **Cyproterone acetate exposure during gestation in mice retards fetal growth.** Physiology & Behavior. 21(4):515-517, 1978.

Pregnant Rockland-Swiss mice were injected with one of seven doses of cyproterone acetate (CA) from day 12 through day 17 of pregnancy. Exposure to CA that blocked masculinization (as indicated by anogenital distance) severely retarded fetal growth. CA also increased the incidence of fetal deaths. CA is thus not recommended for use as an antiandrogen during gestation in mice. 8 references. (Author abstract)

003130 Waldmeier, P. C.; Kam, R.; Stocklin, K. Research Department, Pharmaceuticals Division, CIBA-GEIGY Ltd., Basel, Switzerland **Increased dopamine metabolism in rat striatum after infusions of substance P into the substantia nigra.** Brain Research (Amsterdam). 159(1):223-227, 1978.

The effect of local application of substance P(SP) to the substantia nigra (SN) on the levels of the dopamine metabolites homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC) in the corpus striatum was investigated in female Tif:RAIF (SPF) rats. SP (30mcg/mcl in saline at a rate of 2.34mcl/hour) was infused into the right SN for 15, 30, and 60 minutes. Significant increases of HVA and DOPAC in the ipsilateral striata were found only after 60 minute infusions. The levels of HVA and DOPAC were increased significantly in the ipsilateral striata at cumulative doses of 52.8mcg/hour and 70.4mcg/hour. At higher cumulative doses, the effect of SP was smaller and more variable. These results are compatible with an excitatory SP input on dopaminergic cells in the SN. 21 references.

003131 Waldmeier, Peter C.; Felner, Aina E. Research Department, Pharmaceutical Division, CIBA-GEIGY Limited, Basle, Switzerland **Deprenil: loss of selectivity for inhibition of B-type MAO after repeated treatment.** Biochemical Pharmacology (Oxford). 27(5):801-802, 1978.

The effect of chronic treatment with deprenil, an irreversible selective inhibitor of type B monoamine oxidase (MAO), was examined in female Sprague-Dawley rats. Animals were treated with 1 or 10mg/kg of either deprenil or harmaline, a reversible type A MAO inhibitor, acutely or once daily for 2, 4, 7, or 14 days. Determination of MAO activity in brain and liver revealed that the selectivity for inhibition of type B MAO (phenylethylamine deamination) observed after acute treatment with deprenil diminished progressively in the course of repeated treatment, as inhibition of type A MAO (5-hydroxytryptamine deamination) became more and more effective. This loss of selectivity was more pronounced in brain than in liver, probably as a result of the lower rate of enzyme resynthesis in cerebral tissue. No comparable loss of selectivity was observed after harmaline. 19 references.

003132 Wastek, G.J.; Speth, R.C.; Reisine, T.D.; Yamamura, H.I. Department of Pharmacology, College of Medicine, University of Arizona Health Sciences Center, Tucson, AZ 85724 **The effect of gamma-aminobutyric acid on 3H-flunitrazepam binding in rat brain.** European Journal of Pharmacology (Amsterdam). 50(4):445-447, 1978.

The addition of gammaaminobutyric acid (GABA, 0.1nM-200mcM) resulted in a dose dependent increase in 3H-flunitrazepam binding in several areas of male Sprague-Dawley rat brain. The addition of 200mcM GABA to 3H-flunitrazepam saturation assays significantly increased the affinity of the benzodiazepine receptors for 3H-flunitrazepam in frontal cortex, cerebellum, hippocampus, and corpus striatum, without altering binding capacity. Beta-alanine, a structural analogue of GABA that interacts weakly with the postsynaptic GABA receptor, showed no such effect at similar concentrations, suggesting that the enhancement of affinity of 3H-flunitrazepam binding is specific to GABA. These data indicate that GABA does not interact directly with the 3H-flunitrazepam binding site but may act allosterically to enhance benzodiazepine binding. Alternatively, GABA may decrease the synthesis or release of an endogenous benzodiazepine-like neurotransmitter and thereby reduce the

amount of this substance available to compete with 3H-flunitrazepam at the receptor site. 5 references.

003133 Waymire, Jack C.; Gilmer-Waymire, Katrina; Boehme, Richard E. Department of Psychobiology, University of California, Irvine, CA 92717 **Concomitant elevation of tyrosine hydroxylase and dopamine beta-hydroxylase by cyclic AMP in cultured mouse neuroblastoma cells.** Journal of Neurochemistry (Oxford). 31(3):699-705, 1978.

The effects of cyclic adenosine monophosphate (cAMP) analogues and of phosphodiesterase inhibitors were investigated in neuroblastoma cells (NBD-2) cloned from the mouse C-1300 tumor. Phosphodiesterase inhibitors that elevated cAMP and 8-bromo-cAMP induced large and specific increases in tyrosine hydroxylase (TH) and dopamine-beta-hydroxylase (DBH) activity. Catechol-O-methyl transferase, monoamine oxidase, and aromatic L-amino acid decarboxylase were unaffected by the cAMP altering drugs. Acetylcholinesterase was also unaffected, and only a small increase in choline acetyltransferase was observed. The increases in TH and DBH were similar with respect to dose response relationships and time course of onset. Phosphodiesterase inhibitors that elevated cAMP (papaverine and 4-(3-butoxy-4-methoxy-benzyl)-2-imidazolidinone) elevated TH and DBH, and the doses optimal for elevating cAMP coincided with those optimal for elevating the two enzymes. Theophylline had no effect on cAMP levels or on DBH and TH activity. The changes in protein synthesis rate produced by cAMP altering drugs were temporally distinct from the changes in TH and DBH. Results suggest that the intracellular messenger compound cAMP is involved in the specific regulation of both TH and DBH in adrenergic cells. 39 references. (Author abstract modified)

003134 Weiner, H.; Simpson, C. W.; Thurman, J. A.; Myers, R. D. Department of Biochemistry, Purdue University, West Lafayette, IN 47907 **Disulfiram alters dopamine metabolism at sites in rat's forebrain as detected by push-pull perfusions.** Brain Research Bulletin. 3(5):541-548, 1978.

The effect of disulfiram on the catabolism of dopamine within discrete regions of the male Wistar rat brain was investigated. After a guide cannula was implanted stereotaxically, a given subcortical site was radiolabeled with 14C-dopamine (DA) by microinjecting 2.0mcCi in 2.0mcl. Successive push/pull perfusates collected from each tissue were assayed by paper electrophoresis for the separation of DA metabolites. When disulfiram was given intragastrically in a dose of 200mg, the formation of 3,4-dihydroxyphenyl acetic acid and homovanillic acid was inhibited in perfusates of the caudate nucleus and nucleus accumbens; the proportion of alcohol metabolites did not differ from control level, but the level of aldehyde dehyrogenase decreased by about 50% in these subcortical nuclei. In samples of perfusate obtained from labeled sites within the inferofrontal cortex, pyriform cortex, diagonal band of Broca, lateral posterior caudate nucleus, tuberculum olfactorium, lateral olfactory tract, or olfactory nuclear complex, the proportion of DA metabolites remained stable. A low rate of deamination of exogenously injected DA occurred within perfusion sites in the ventrobasal forebrain, whereas an intermediate rate of deamination was noted in samples from more dorsal loci. 34 references. (Author abstract modified)

003135 Weiss, G. B.; Wheeler, E. S. Dept. of Pharmacology, University of Texas Health Sciences Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX 75235 **Inhibition of 45Ca movements by lowered temperature or lanthanum in rat brain slices.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 233(1):4-20, 1978.

Different components of 45Ca movements in rat cortex, striatum, and hypothalamus slices were delineated by conditions and ions which selectively alter Ca2 uptake, binding or extrusion. Equilibration of 45Ca was qualitatively similar in all three tissues and was attained within 30-60 min. The 45Ca tissue/medium ratios obtained in 1.5mM Ca2 solutions were increased 15% to 30% in 0.1mM Ca2 solutions and doubled in 0-Ca solutions. Lowering the temperature to 0 degrees C increased 45Ca uptake into the slower washout component and markedly decreased 45Ca efflux. Exposure to 1.5mM La3 decreased both 45Ca uptake and efflux. The inhibitory effects of 0 degrees C and La3 decreased both 45Ca uptake and efflux. The inhibitory effects of 0 degrees C and La3 on 45Ca efflux were additive. Uptake of 45Ca in slices incubated in 1.5mM Sr2 substituted (0-Ca) solutions was more similar to that in 0-Ca solutions than in 1.5mM Ca2 solutions. These results indicate that Ca2 distribution is qualitatively similar in slices from different rat brain areas, loss of 45Ca is an energy dependent process which is at least partially coupled to Ca2, and Sr2 does not prevent the major portion of 45Ca uptake at cellular binding sites. Use of 0 degree C and La3 to inhibit discrete components of Ca2 fluxes in rat brain area slices provides a basis for investigation of the mechanisms by which other agents can alter Ca2 distribution in the central nervous system. 32 references. (Author abstract)

003136 Wesche, David; Hollt, Volker; Herz, Albert. Abteilung fur Neuropharmakologie, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **Radioimmunoassay of enkephalins: regional distribution in rat brain after morphine treatment and hypophysectomy.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 301(1):79-82, 1977.

Methionine-enkephalin and leucine-enkephalin levels were determined in various areas of the brains of female Sprague-Dawley rats, using highly sensitive and highly specific antisera. The highest content of both enkephalins was found in the striatum and hypothalamus, whereas low levels were found in the hippocampus, cerebellum and cortex. The ratio of methionine-enkephalin/leucine-enkephalin was about 3. Enkephalin levels in the brain regions examined were not significantly altered by hypophysectomy, chronic or acute morphine treatment, or precipitated withdrawal from morphine. 15 references. (Author abstract modified)

003137 Westermann, K. H.; Funk, K. F. Institute of Pharmacology and Toxicology, Medical Academy "Carl Gustav Carus," Dresden, Germany **pharmacological evidence for dopaminergic pallido-striatal interaction.** Pharmacology Biochemistry and Behavior. 8(6):645-649, 1978.

The effects of nigrostriatal axotomy compared to the effects of pallidal lesions on striatal dopamine content were studied to determine the functional significance of simple and combined lesions for rotational behavior (circling, turning) appearing in unilateral nigrostriatal lesioned rats following dopaminergic receptor stimulating agents. The contents in dopamine (DA) and 3,4-dihydroxyphenylacetic acid (DOPAC) of neostriatum nucleus caudatoputamine (NCP) and paleostriatum globus pallidus (GP) were measured after transection of the capsula interna (CI) or after injection of 6-hydroxydopamine (6-OHDA) into the GP of one side. The circling behavior of the lesioned animals following apomorphine was also studied. It was found that 6-OHDA as well as transection decreased the contents in DA and DOPAC in NCP and GP significantly. Following both treatments, DA levels in neostriatum were lowest. Nigro-neostriatal pathway lesioned animals rotated toward the side of lesion after apomorphine, whereas GP lesioned animals rotated toward the intact side. In animals with both GP and substantia nigra (SN) lesions at one side, turnings of similar intensity toward both sides were seen. In intact rats DA injections into SN or NCP

exhibited contralateral; injections into GP exhibited ipsilateral rotations. The results strengthen the hypothesis on the participation of GP in the regulation of neostriatal content of DA and show the interaction of the hypothetical dopaminergic pallidostriatal pathway with nigro-neostriatal pathways. 41 references. (Author abstract modified)

003138 Whitaker, Patricia M.; Seeman, Philip. Department of Pharmacology, Medical Sciences Building, University of Toronto, Toronto, M5S 1A8, Canada **High-affinity 3H-serotonin binding to caudate: inhibition by hallucinogens and serotoninergic drugs.** Psychopharmacology (Berlin). 59(1):1-5, 1978.

The specific binding of 3H-serotonin to calf caudate homogenate was studied. The dissociation constant was 2nM and the number of specific sites was 14fM/mg protein. Of the many drugs tested, only serotonin agonists and antagonists inhibited specific 3H-serotonin binding. Results indicate that the concentrations for 50% inhibition of 3H-serotonin binding by serotoninergic agonists were bufotenin, 6nM; 5-methoxytryptamine, 12nM; psilocin, 35nM; dimethyltryptamine, 220nM; and tryptamine, 270nM. The concentrations for the antagonists were lysergic acid diethylamid, 9.5nM ; methysergide, 16nM; and metergoline, 25nM. 14 references. (Author abstract modified)

003139 Wilk, Sherwin; Stanley, Michael. Department of Pharmacology, Mount Sinai School of Medicine, CUNY, Fifth Avenue and 100 St., New York, NY 10029 **Clozapine concentrations in brain regions: relationship to dopamine metabolite increase.** European Journal of Pharmacology (Amsterdam). 51(2):101-107, 1978.

The effect of intraperitoneal administration of 10, 20, or 40mg/kg clozapine on levels of clozapine and 3,5,3,4-dihydroxyphenylacetic acid (DOPAC) in rat striatum and tubercle olfactorium (TO) was studied using a gas chromatographic technique. One hour after clozapine injection, the concentration of drug increased in proportion to the dose in both striatum and TO. The percent increase in DOPAC in both areas was related to the clozapine concentration in a typical dose response manner and was greater in striatum than in TO. A relatively high concentration of clozapine (40mcM) was required to produce a half maximal elevation of DOPAC. Striatal clozapine levels were similar in acutely and chronically treated animals. The concentrations of clozapine in striatum and TO reflect the dose injected and do not account for its atypical properties. 24 references. (Author abstract modified)

003140 Wong, Chak-Lam; Bentley, Geoffrey A. Department of Pharmacology, Monash University, Clayton, Victoria, 3168, Australia **The role of the cholinergic system in the development of increased naloxone potency in mice.** European Journal of Pharmacology (Amsterdam). 50(3):221-230, 1978.

Pretreatment with the anticholinesterase (antiChE) drugs tacrine or physostigmine augmented the antinociceptive potency of morphine given 3 hours later in male Swiss mice, but had no effect on the antagonist potency of naloxone. Pretreatment with either of these antiChE drugs together with morphine not only augmented the potency of a subsequent dose of morphine, but also enhanced the antagonist potency of naloxone to a greater extent than pretreatment with morphine alone. Neostigmine did not affect the potency of morphine or naloxone, suggesting that this phenomenon involves central cholinergic mechanisms. Atropine prevented the increase in naloxone potency caused by morphine pretreatment and greatly reduced the effect of morphine plus the antiChE drugs. The development of acute morphine dependence, as tested by naloxone precipitated jumping, was not affected by antiChE drugs but was increased by pretreatment with atropine sulfate or atropine methyl nitrate. It is concluded that the increase in naloxone potency following morphine pretreatment involves both a cholinergic mechanism and narcotic analgesic action. This phenomenon does not appear to be related to the development of acute tolerance or acute dependence. 30 references. (Author abstract modified)

003141 Wong, S. C.; Yeung, Y. G.; Yeung, D. Department of Biochemsitry, University of Hong Kong, Hong Kong **Effects of morphine on isoenzymes of pyruvate kinase and tyrosine aminotransferase in rat.** Biochemical Pharmacology. 27(9):1347-1351, 1978.

The acute and chronic effects of morphine on isoenzymes of pyruvate kinase and tyrosine aminotransferase in albino rat liver were studied in vivo. Acute administration of morphine inhibits the L-type pyruvate kinase but increases forms II, III, and IV of tyrosine aminotransferase in rats given a single intraperitoneal injection of morphine 6 hours prior to sacrifice; both effects are lost after 24 hours. Morphine starts to regain its stimulatory effect on tyrosine aminotransferase at 48 hours and reaches a maximum at 72 hours. Chronic morphinization leads to similar changes in the total activities of pyruvate kinase and tyrosine aminotransferase, but the change in isoenzyme pattern of tyrosine aminotransferase concerns only forms II and III. These results confirm the hydrocortisone/like property of morphine and indicate that morphine may enhance glucogenesis in vivo. 31 references. (Author abstract)

003142 Yaksh, Tony L. Department of Medical Research, Mayo Clinic, Rochester, MN 55901 **Opiate receptors for behavioral analgesia resemble those related to the depression of spinal nociceptive neurons.** Science. 199 (4334):1231-1233, 1978.

With naloxone as atagonist, a dose ratio analysis of the depression by morphine of nociceptive neurons in the dorsal horn of the unanesthetized, decerebrate spinal cat reveals that this opiate depression of single unit activity has the same pharmacological properties as observed with morphine analgesia. This suggests that the opiate receptor, mediating the observed cellular depression, and those mediating analgesia are presumably the same. 15 references. (Author abstract)

003143 Yaksh, Tony L.; Fredrickson, Robert C. A.; Huang, Sung P.; Rudy, Thomas A. Department of Neurosurgery, Mayo Clinic, Rochester, MN 55901 **In vivo comparison of the receptor populations acted upon in the spinal cord by morphine and pentapeptides in the production of analgesia.** Brain Research (Amsterdam). 148(2):516-520, 1978.

A dose ratio analysis of two enkephalin pentapetides, Met5-enkephalin amide (ENKAMIDE) and D-Ala2-Met5-enkephalin amide (DALA), was performed. ENKAMIDE and DALA (10microl) were injected in the spinal subarachnoid space of rats and followed by intraperitoneal injection of naloxone. Animals were tested twice prior to injection of the drugs and twice at the time of peak effect on the tail flick test. Dose response curves for DALA, ENKAMIDE, and morphine, in the presence of increasing doses of naloxone, indicate that DALA was 22 times and ENKAMIDE 0.06 times as potent as morphine. The slope of the dose ratio curve obtained using DALA was virtually identical to that obtained with morphine, providing the strongest evidence to date that the pentapeptides, in-vivo, act on the same receptor population as do the exogenous opiates. The slope of the dose ratio curve obtained with ENKAMIDE differed from that obtained with either morphine or DALA, but this variation does not necessarily indicate a different receptor interaction. 21 references.

003144 Yamamoto, M. Research Laboratories, Yamanouchi Pharmaceutical Co., Ltd., Azusawa, Itabashi-Ku, Tokyo 174, Japan **Pharmacological studies of central action of L-5-hydroxy-**

tryptophan in intact or tetrabenazine-pretreated cats. Current Therapeutic Research. 23(4):509-524, 1978.

The effect of L-5-hydroxytryptophan (L-5HTP) on various regions of the brain was investigated in intact or tetrabenazine treated cats. In the intact cats, L-5HTP inhibited the electroencephalographic responses induced by the electrical stimulation of the caudate nucleus and the mesencephalic reticular formation and suppressed the pressor response induced by the electrical stimulation of the posterior hypothalamus. L-5HTP augmented the duration of afterdischarges induced by electrical stimulation of the cerebral cortex, the hippocampus, and the amygdaloid nucleus. In the pretreated cats, the augmentative effect on the amygdaloid afterdischarges and the depressor effect on the hypothalamic pressor response were weak compared with those in the intact cat. The sites of central action of L-5HTP are discussed in relation to brain amine levels. 15 references. (Author abstract)

003145 Yavin, Ziva; Biegon, Anat; Segal, Menachem; Samuel, David. Weizmann Institute of Science, Isotope Department, Rehovot, Israel **The in vivo binding of (3H)-desipramine and (3H)-chlorpromazine to areas in the rat brain.** European Journal of Pharmacology (Amsterdam). 51(2):121-127, 1978.

The distribution of (3H)-desipramine (DMI) and (3H)-chlorpromazine (CPZ) in male Wistar rat brain was determined by the incorporation of radioactivity into various regions of the brain and by autoradiography of transverse cryostat sections. The label from (3H)-DMI was rapidly distributed in all brain regions, reaching peak levels within 30 minutes and considerably decreasing 1-4 hours after injection. Following the selective destruction of catecholaminergic nerve terminals by intracerebral administration of 6-hydroxydopamine, a marked reduction in the incorporation of DMI, but not of CPZ, was evident in all brain areas examined. The autoradiographed sections clearly demonstrated a preferential uptake of both drugs by the caudate nucleus. These findings suggest that DMI might be largely bound to presynaptic dopamine and norepineprhine terminals, while CPZ binding involves postsynaptic sites. 26 references. (Author abstract)

003146 Yehuda, Shlomo; Frommer, Reuven. Psychopharmacology Laboratory, Department of Psychology, Bar-Illan University, Ramat-Gan, Israel **Effects of d-amphetamine on the set point of the thermoregulatory system in rats.** Psychopharmacology (Berlin). 57(3):249-252, 1978.

The effect of d-amphetamine on the set point of the thermoregulatory system was determined in male Sabra rats. Animals were tested at various ambient temperatures (4-20 degrees C), with their tails exposed to temperatures ranging from 0-15 degrees C. Exposure of the tail to temperatures lower than that sensed by the rest of the body caused an increase in body temperature; this effect was enhanced by pretreatment with d-amphetamine. Control rats perceived any temperature below 20 as cold, while amphetamine treated animals reacted to water temperature of 10 as below normal and to 15 as above normal. Results indicate that amphetamine lowers the internal thermoregulatory set point. 11 references. (Author abstract modified)

003147 Young, Simon N.; St-Arnaud-McKenzie, Danielle; Sourkes, Theodore L. Laboratory of Neurochemistry, Department of Psychiatry, McGill University, Montreal, Quebec, Canada H3A 1A1 **Importance of tryptophan pyrrolase and aromatic amino acid decarboxylase in the catabolism of tryptophan.** Biochemical Pharmacology (Oxford). 27(5):763-767, 1978.

The effect of benserazide, an inhibitor of aromatic amino acid decarboxylase (AADC), on the breakdown of tryptophan by AADC and tryptophan pyrrolase was assessed in male Sprague-Dawley rats. Benserazide potentiated the rise of plasma tryptophan in rats given a tryptophan load and inhibited the release of labeled carbon dioxide (14C02) in animals given carboxyl labeled tryptophan. These results can be explained by the ability of benserazide to inhibit tryptophan pyrrolase, the most important enzyme catabolizing tryptophan. Direct decarboxylation was not a quantitatively important pathway of tryptophan catabolism, and carboxyl labeled tryptophan was metabolized to 14CO2 primarily by the pyrrolase pathway. These findings have implications for the clinical use of tryptophan as an antidepressant. Pyridoxine, which is often given with tryptophan in clinical use, can activate AADC. However, pyridoxine did not inhibit the rise of plasma tryptophan in rats given a tryptophan load and is unlikely to antagonize the therapeutic effect of tryptophan. It may be possible to potentiate the therapeutic effect of tryptophan by administering it with benserazide to inhibit its peripheral catabolism through the pyrrolase pathway. 24 references. (Author abstract)

003148 Zabik, Joseph E.; Liao, Shu-Shen; Jeffreys, Matthew; Maickel, Roger P. Section on Pharmacology, Medical Science Program, Indiana University School of Medicine, Bloomington, IN 47401 **The effects of DL-5-hydroxytryptophan on ethanol consumption by rats.** Research Communications in Chemical Pathology and Pharmacology. 20(1):69-78.

The effects of DL-5-hydroxytryptophan (5-HTP) on ethanol consumption by rats were examined. Male Sprague-Dawley rats were offered access to either distilled water or a 12% v/v solution of ethanol as their only fluid during a 1 hour period daily. After daily fluid consumption had achieved a stable baseline, either distilled water or 5-HTP in doses of 50, 100, or 200 mg/kg was injected intraperitoneally 1 hour prior to the drinking session. While each of the three doses of 5-HTP caused a significant reduction in ethanol intake, distilled water had no effect. Water consumption was unaffected by 5-HTP or distilled water injections. Varying the pretreatment interval from 0.5, 1, 4 to 8 hours for the 100 mg/kg 5-HTP dose resulted in a significant decrease in ethanol consumption at 0.5and 1 hour pretreatment intervals only. In approximately 25% of the rats tested, 5-HTP resulted in a prolonged rejection of ethanol so severe that it resulted in death. Selected rats offered water during this ethanol rejection period readily drank it and survived. 15 references. (Author abstract modified)

003149 Zahniser, N. R.; Katyal, S. L.; Shih, T.-M.; Hanin, I.; Moossy, J.; Martinez, A. J.; Lombardi, B. Dept. of Pharmacology, University of Colorado Medical Center, Denver, CO 80220 **Effects of N-methylaminoethanol, and N,N-dimethylaminoethanol in the diet of pregnant rats on neonatal rat brain cholinergic and phospholipid profile.** Journal of Neurochemistry (Oxford). 30(6):1245-1252, 1978.

In an attempt to study alterations in the neonatal rat brain cholinergic and phospholipid system due to the diet of the mother dam pregnant Sprague-Dawley rats were fed for 15 days predelivery until 15 days postpartum a choline (Ch) deficient diet (CD diet) or a CD diet supplemented with 0.8% Ch-Cl (CS), 1% N-methylaminoethanol (MME) or 1% N,N-dimethylaminoethanol (DME). Gestation and parturition of the pregnant rats proceeded normally. However, all the pups born of dams fed the MME diet, and most of those born of dams fed the DME diet, died within 36 hours of birth. No histological or cytological alterations were detected in the brain of the pups. Levels of Ch and acetylcholine were elevated in the brain of pups born of dams fed the MME and DME diets, but not the CS diet. The content of total phospholipids in the brain of the pups was not altered by the diet fed to the dams. However, the phosphatidyl-Ch and phosphatidylaminoethanol contents in the brain of the MME and DME exposed pups were markedly re-

duced. At the same time, significant amounts of DME, phosphatidyl-N-monomethylaminoethanol and of phosphatidyl-N,N-dimethylaminoethanol were present in the same brain areas. These results are evaluated and discussed in terms of providing a cause for the death of the MME and DME exposed neonatal rats. 41 references. (Author abstract)

04 MECHANISM OF ACTION: BEHAVIORAL

003150 Ho, B. T. Texas Research Institute of Mental Sciences, 1300 Moursund Avenue, Houston, TX 77030 **Characterization of discriminative stimulus properties of psychomotor stimulants.** Psychopharmacology (Berlin). 58(2):6, 1978.

At the First International Symposium of Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, studies of the discriminative stimulus properties of psychomotor stimulants were reported. Amphetamine, cocaine, and methylphenidate showed cross-generalization, indicative of the involvement of a common mechanism in serving as stimuli. Intraventricular administration of the drugs indicated that the discriminative behavior was mediated by the CNS. Use of various agonists and antagonists of aminergic systems showed that the discriminative properties of psychomotor stimulants are mediated by a dopaminergic mechanism. (Author abstract modified)

003151 Abel, Ernest L. Research Institute on Alcoholism, 1021 Main St., Buffalo, NY 14203 **Effects of ethanol and pentobarbital in mice of different ages.** Physiological Psychology. 6(3):366-368, 1978.

The effects of ethanol and pentobarbital on sleep time and general motor activity were examined in mice of two different ages. Older animals slept twice as long as younger animals following injection of ethanol (4g/kg), although blood alcohol concentrations at time of awakening were not significantly different. Older mice also slept approximately twice as long as younger mice following injection of pentobarbital Na (50mg/kg). Ethanol (3g/kg) depressed gross motor activity of older animals more than younger animals. When tested for their preference for various concentrations of ethanol vs. water, younger animals exhibited a greater preference than older animals at all but two of the concentrations tested. 22 references. (Author abstract modified)

003152 Aceto, Mario D.; Carchman, Richard A.; Harris, Louis S.; Flora, Roger E. Department of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Caffeine elicited withdrawal signs in morphine-dependent rhesus monkeys.** European Journal of Pharmacology (Amsterdam). 50(3):203-207, 1978.

The effects of caffeine in noraml and morphine dependent monkeys were studied. Subcutaneous administration of caffeine (4.0-32.0mg/kg) produced most of the signs commonly seen after naloxone (0.05mg/kg) in morphine dependent rhesus monkeys, including lying on side or abdomen, avoiding contact, vocalizing, crawling or rolling, restlessness or pacing, tremors, retching, vomiting, coughing, rigid abdomen, and salivation. In preliminary studies in naive monkeys, caffeine produced some withdrawal signs, but the results were equivocal. Sodium benzoate (32mg/kg) also elicited some withdrawal signs in morphine dependent monkeys but few signs were seen in naive monkeys. Caffeine was about 10 times more active than sodium benzoate in inhibiting cyclic adenosine monophosphate (cAMP) phosphodiesterase activity in a neuroblastoma cell whole homogenate assay. 16 references. (Author abstract modified)

003153 Ader, Robert; Grota, Lee J.; Buckland, Robert. Dept. of Psychiatry, University of Rochester Medical Center, Rochester, NY 14642 **Effects of adrenalectomy on taste aversion learning.** Physiological Psychology. 6(3):359-361, 1978.

The effects of adrenalectomy on the acquisition of a drug induced taste aversion were examined. Adrenalectomized (ADX) rats were maintained on a saline drinking solution and daily subcutaneous injections of low doses of dexamethasone plus aldosterone. Sham operated control and ADX animals were conditioned by pairing consumption of a saccharin flavored drinking solution with the intraperitoneal injection of cyclophosphamide. Nonconditioned animals received only cyclophosphamide. An attenuation of the neophobic response to the initial exposure to saccharin in ADX animals was attributed to the need to consume salt in these animals. ADX and control groups displayed a significant aversion to saccharin presented 3 days after conditioning. Results indicate that the release of adrenocortical steroids in response to the conditioned stimulus or the unconditioned stimulus is not a necessary condition for the acquisition of a taste aversion. 17 references. (Author abstract modified)

003154 Aigner, Thomas G.; Balster, Robert L. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **Behavioral effects of chronic oral administration of levo-alpha-acetylmethadol in the rat.** Pharmacology Biochemistry and Behavior. 8(5):593-596, 1978.

Levo-alpha-acetylmethadol in sucrose solution or sucrose solution alone was administered to rats in their drinking water for 24 days. Behavioral effects during chronic drug administration and during 8 days of withdrawal were studied using behavior controlled by a fixed-interval schedule of food reinforcement. Response rate and number of reinforcements decreased during drug administration. During withdrawal, response rates were greater than predrug control rates. Body weights of treated animals remained stable during drug administration but decreased by about 25% during withdrawal. There were no significant differences in volume of fluid consumed by the treated and control groups. 13 references. (Author abstract modified)

003155 Aigner, Thomas G.; Balster, Robert L. Department of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Choice behavior in rhesus monkeys: cocaine versus food.** Science. 201(4355):534-535, 1978.

A choice behavior experiment in which rhesus monkeys were allowed to choose between intraveneous injections of cocaine and small amounts of food is presented. The relative reinforcing strength of cocaine was qualitatively measured; the monkeys were allowed to choose an interveneous injection of cocaine or a small amount of food by pressing a lever. It is demonstrated that rhesus monkeys, in a nonforced situation, will consistently choose intraveneous cocaine over food, even after several days of reduced food intake. 12 references. (Author abstract)

003156 Aigner, Thomas G.; Ford, Robert D.; Balster, Robert L. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **Levo-alpha-acetylmethadol and metabolites: some effects on schedule-controlled behavior in the rat.** Pharmacology Biochemistry and Behavior. 8(6):735-737, 1978.

The effects of levo-alpha-acetylmethadol (LAAM) and its metabolites, levo-alpha-noracetylmethadol (NAM) and levo-alpha-dinoracetylmethadol (NNAM) on schedule controlled behavior were studied and compared to the prototype opiate, morphine. Acute intraperitoneal administration of LAAM, NAM, NNAM and morphine resulted in a dose related decrement in response rate. The metabolites had approximately three to four times the potency of the parent compound, which had approximately five times the potency of morphine. Data obtained from cumulative response records suggest that the onset of effects for the meta-

bolites is more rapid than for the parent compound. 12 references. (Author abstract modified)

003157 Albert, D. J.; Wong, R. C. K. Department of Psychology, University of British Columbia, Vancouver, British Columbia, Canada **Interanimal agression and hyperreactivity following hypothalamic infusion of local anesthetic in the rat.** Physiology & Behavior. 20(6):755-761, 1978.

Hyperreactivity and agression were studied with temporary lesions made by infusing a local anesthetic (2% lidocaine) into the medial hypothalamus or adjacent areas in male hooded rats. Bilateral infusions of 1 mel, at a rate of 1 mel/3 minutes, were made every 5 minutes over a 20 minute period. Muricide, intermale aggression, and reactivity to the experimenter were assessed following each injection. Each of these behaviors was produced by injections along the descending columns of the fornix, in the anterior one third of the ventromedial hypothalamic nucleus, and more posteriorly between the ventromedial nucleus and the fornix. The appearance of hyperreactivity, muricide, and intermale aggression were positively correlated with one another. The time of their appearance during the infusion period was similar for different infusion sites along the anterior/posterior length of the medial hypothalamus. Infusion of lidocaine into the medial forebrain bundle did not induce an increase in these behaviors. It is suggested that two systems, one modulating interanimal aggression and another modulating reactivity, are affected by these injections. The systems, while distinct, overlap in the medial hypothalamus and are not localized solely in the ventromedial nucleus. 26 references. (Author abstract modified)

003158 Alexander, Bruce K.; Coambs, Robert B.; Hadaway, Patricia F. Department of Psychology, Simon Fraser University, Burnaby, British Columbia, Canada V5A 1S6 **The effect of housing and gender on morphine self-administration in rats.** Psychopharmacology (Berlin). 58(2):175-179, 1978.

To determine the effect of housing conditions on morphine self-administration, Wistar rats isolated in standard laboratory cages and rats living socially in a large open box were given morphine in solution (0.5mg/ml) as their only source of fluid for 57 days. Rats were then exposed to a series of 3 day cycles, previously shown by Nichols to increase self-administration of morphine in caged rats. On morphine/water choice days late in the period of forced consumption, between the Nichols cycles, and during a subsequent period of abstinence, the isolated rats drank significantly more morphine solution than the social rats, and females drank more morphine solution than males. During the 4 choice days in the Nichols Cycle Period, the isolated rats increased consumption and socially housed rats decreased consumption. 18 references. (Author abstract modified)

003159 Alexander, George J.; Alexander, Rita B. New York State Department of Mental Hygiene, Neurotoxicology Research Unit, 722 West 168th Street, New York, NY 10032 **Alcohol consumption in rats treated with lithium carbonate or rubidium chloride.** Pharmacology Biochemistry and Behavior. 8(5):533-536, 1978.

The effects of lithium carbonate and rubidium chloride on alcohol consumption were examined in rats. The animals were injected for 5 days with lithium, rubidium, or placebo and were offered a free choice between tap water and a 10% ethanol solution in the absence of reinforcement. The lithium treated group consumed 25% more liquid per day but chose to take 14.5% less alcohol than controls. By contrast, the rubidium treated rats consumed 15% less liquid but 70% more alcohol than control animals. Rudibium treated rats were strikingly more active than the other two groups: their motility index was 60.0, compared to 33.6for lithium treated and 29.4for control rats. Serum glucose and urea nitrogen concentration were not significantly affected by the treatment, but serum alcohol content was low in lithium treated rats and high in rubidium treated rats. 17 references. (Author abstract modified)

003160 Ando, K.; Yanagita, T. Preclinical Research Laboratories, Central Institute for Experimental Animals, 1433 Nogawa, Takatsu-ku, Kawasaki, Japan 211 **The discriminative stimulus properties of intravenously administered cocaine in rhesus monkeys.** Psychopharmacology (Berlin). 58(2):3, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, the discriminative stimulus properties of intravenously administered cocaine in two rhesus monkeys were reported. Discriminated choice responding between cocaine (0.1mg/kg) and saline reached an 80% correct criterion in a two lever choice procedure reinforced under a fixed ratio 8 schedule. Test infusions of cocaine (0.025-0.05mg/kg), morphine (0.05-0.1mg/kg), d-amphetamine (0.0125-0.1mg/kg), and methamphetamine (0.025-0.1mg/kg) produced dose related responding on the cocaine lever in both monkeys tested. Infusions of chlorpromazine (0.05-0.4mg/kg), alcohol (100-400mg/kg), and pentobarbital-Na (4-16mg/kg) produced responding on the saline lever in both monkeys. Results indicate that rhesus monkeys may possess susceptibility similar to that of man in discriminating the subjective effects of the morphine/amphetamine group from those of the pentobarbital/chlorpromazine/alcohol group. (Author abstract modified)

003161 Apfelbach, R. Universitat Tubingen, Lehrstuhl fur Zoophysiologie, Morgenstelle 28, D-7400 Tubingen, Germany **Instinctive predatory behavior of the ferret (Putorius putorius furo L.) modified by chlordiazepoxide hydrochloride (Librium).** Psychopharmacology (Berlin). 59(2):179-182, 1978.

The effects of chlordiazepoxide hydrochloride (lmg/kg) on the instinctive predatory behavior of the ferret (Putorius putorius furo L.)were investigated. Intramuscular injections of chlordiazepoxide appeared to make the ferrets less cautious about attacking relatively large prey rather than improving their predatory behavior. The drug produced no change in behavior when ferrets were presented with rats weighing less than 40% of the ferret but decreased the amount of time and number of bites necessary to kill rats weighing more than 40% of the ferret. Rats were more successful in biting drugged ferrets than normal ones. It is concluded that chlordiazepoxide disinhibited the ferrets when they were presented with large rats, which they normally attack more cautiously. The possibility of a disinhibiting effect of chlordiazepoxide should be considered in treating patients who may show aggressive or hostile behavior. 20 references. (Author abstract modified)

003162 Babbini, M.; Gaiardi, M.; Bartoletti, M. Institute of Pharmacology, University of Bologna, Bologna, Italy **Motility effects of methamphetamine in rats chronically treated with morphine.** Neuropharmacology (Oxford). 17(11):979-983, 1978.

The effects of methamphetamine (MAMPH) were studied in naive male Sprague-Dawley rats and in rats previously treated daily with 20mg/kg morphine for 26 days. The animals were tested in jiggle cage actographs for 7 hours after MAMPH treatment, and data related to the motility scores were analyzed as response surfaces by analysis of variance. Chronic morphine treatment altered neither the response surface of MAMPH effect upon activity nor the median effective dose values for the appearance of stereotyped behavior. The data do not support the hypothesis of a dopamine receptor supersensitivity during chronic morphine treatment, but suggest that presynaptic changes in dopamine turnover can occur when rats are treated

repeatedly with opiates. 31 references. (Author abstract modified)

003163 Barry, H., III; Krimmer, E. C. Department of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15261 **Similarities and differences in discriminative stimulus effects of chlordiazepoxide, pentobarbital, ethanol, and other sedatives.** Psychopharmacology (Berlin). 58(2):3, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Beigium, July 1978, similarities and differences in discriminative stimulus effects of chlordiazepoxide, pentobarbital, ethanol, and other sedatives were discussed. Similar discriminative stimulus attributes shared by these drugs appear to be related to a sedative, antianxiety reducing effect. The discriminative drug stimulus is strongest at doses causing conspicuous muscular flaccity and can be antagonized by bemegride, a central stimulant. Behavioral depression does not account for the discriminative sedative stimulus, however. The discriminative drug response occurs at low and moderate doses of pentobarbital and chlordiazepoxide and does not generalize to behaviorally depressant doses of other types of drugs. The pentobarbital stimulus generalizes consistently to ethanol only under conditions of intense stress or conflict. The technique of training animals to discriminate between equivalently potent doses of two sedative agents has demonstrated qualitatively differential stimulus attributes of pentobarbital and ethanol. (Author abstract modified)

003164 Barthalmus, George T.; Leander, J. David; McMillan, D. E. Department of Zoology, North Carolina State University, Raleigh, NC 27607 **Combined effects of ethanol and diazepam on performance and acquisition of serial position sequences by pigeons.** Psychopharmacology (Berlin). 59(1):101-102, 1978.

The effects of diazepam and ethanol, alone and in combination, were studied in pigeons responding under acquisition and performance chain schedules. Both diazepam and ethanol increased the number of pecks on the incorrect key. Under the acquisition schedule both diazepam and ethanol increased errors at doses lower than those under the performance schedule. Under both schedules, effects of combinations of ethanol and diazepam were usually greater than the sum of the effects of the individual drugs. 9 references. (Author abstract modified)

003165 Bass, Michael B.; Friedman, Howard J.; Lester, David. Center of Alcohol Studies, Rutgers University, New Brunswick, NJ 08903 **Antagonism of naloxone hyperalgesia by ethanol.** Life Sciences. 22(21):1939-1946, 1978.

Male Sprague-Dawley rats were pretreated by intraperitoneal with ethanol (1.25g/kg) or saline 5 minutes prior to subcutaneous injection of saline or naloxone hydrochloride (0.1or 0.2mg/kg). Beginning 15 minutes after the second injection, the rats were given five noncontingent 0.5second footshocks at 0.6, 0.8, and 1.3mA in a random order on a variable time 1 minute schedule. The amplitude of the startle response, number of audible vocalizations, and extent of overt movements were recorded. Ethanol significantly reduced startle response amplitude and overt movements at 0.8and 1.3mA and naloxone failed to antagonize these indices of ethanol analgesia. Naloxone itself had no effect on overt movements, but it significantly increased startle response amplitude and vocalizations at 1.3mA; ethanol prevented these naloxone induced increases. Possible mechanisms of ehtanol effects on endorphin systems are considered. 26 references. (Author abstract modified)

003166 Bean, Noel J.; Loman, Kris; Conner, Robert. Department of Psychology, Bowling Green State University, Bowling Green, OH 43403 **Effects of benzazepine (Sch-12679) on shock-induced fighting and locomotor behavior in rats.** Psychopharmacology (Berlin). 59(2):189-192, 1978.

The effects of benzazepine (Sch-12679) and the extent to which any effects could be accounted for on the basis of drug induced debilitation of motoric capacities was examined. Benzazepine was found to reduce the shock induced fighting behavior of male Long-Evans rats in a dose dependent fashion. However, the drug also impaired both locomotor behavior and rotorod performance. These results suggest that the aggression suppressive effects of benzazepine may be mediated by drug induced sedation. 7 references. (Author abstract modified)

003167 Beattie, Michael S.; Gray, Thackery S.; Rosenfield, John A.; Meyer, Patricia M.; Meyer, Donald R. Ohio State University, Columbus, OH 43212 **Residual capacity for avoidance learning in decorticate rats: enhancement of performance and demonstration of latent learning with d-amphetamine treatments.** Physiological Psychology. 6(3):279-287, 1978.

To determine if performance can be facilitated via pharmacological injections after removal of the neocortex, unoperated and decorticated rats were trained on a shuttlebox conditioned avoidance response (CAR) according to a sequential schedule of d-amphetamine sulfate (1.Omg/kg) or vehicle injections. Unoperated rats acquired and retained the CAR regardless of drug conditions, with amphetamine tending to increase performance. Amphetamine enhanced locomotor activity in unoperated and operated rats under all conditions. Decorticate rats failed to show evidence of acquisition during initial training whether given amphetamine or vehicle injections. However, amphetamine resulted in dramatic increases in CAR performance only in decorticates which had no previous experience with the drug. Return to the vehicle alone condition was accompanied by returns to low levels of responding. The rapid performance increments and their state dependent nature suggested not only that rats with neocortical removals could acquire a CAR, but that such animals, trained without drug treatments, can acquire information about the CAR situation which they are unable to employ successfully, and that these latent traces can be expressed under the facilitatory effects of amphetamine. 26 references. (Author abstract)

003168 Bergmann, F.; Feldberg, W. Dept. of Pharmacology, Hebrew University, Hadassah Medical School, Jerusalem, Israel **Effects of propylbenzilylcholine mustard on injection into the liquor space of cats.** British Journal of Pharmacology (London). 63(1):3-6, 1978.

The effects of propylbenzilylcholine mustard injected into the cannulated cerebral ventricles and cisterna magna of unanesthetized cats were determined. Ventricular injections produced extreme motor excitation, vocalization, shivering leading to fever, tachypnoea, panting, piloerection, and salivation, while cisternal injections produced vigorous scratching bouts. Similar injections of atropine produced none of these effects. All the effects were suppressed by anesthetizing doses of pentobarbitone sodium injected intraperitoneally. 13 references. (Author abstract)

003169 Bhargava, Hemendra N. Department of Pharmacognosy and Pharmacology, College of Pharmacy, University of Illinois Medical Center, Chicago, IL 60612 **The effects of divalent ions on morphine analgesia and abstinence syndrome in morphine-tolerant and -dependent mice.** Psychopharmacology (Berlin). 57(2):223-225, 1978.

The effects of intracerebrally administered copper on morphine analgesia in naive and morphine dependent mice are explored. The stereotyped jumping response precipitated by naloxone was inhibited by copper in morphine dependent mice, but copper failed to affect other abstinence signs. When abstinence

was precipitated with a partial antagonist, nalorphine, stereotyped jumping was not inhibited by either calcium or copper. These modifications of narcotic effects by copper were produced without alterations in the brain disposition of morphine. Total radioactivity in the brain following radioactive naloxone administration was not altered. 13 references. (Author abstract)

003170 Bhargava, Hemendra N. Department of Pharmacognosy and Pharmacology, College of Pharmacy, University of Illinois at the Medical Center, Chicago, IL 60612 **The effects of naltrexone on the development of physical dependence on morphine.** European Journal of Pharmacology (Amsterdam). 50(3):193-202, 1978.

The effects of naltrexone on the development of physical dependence on morphine were studied. A single intraperitoneal injection of 20mg/kg naltrexone partially inhibited the development of physical dependence on morphine in male Swiss-Webster mice made dependent by implantation of a 75mg morphine pellet for 3 days. This effect was evidenced by an increase in the median effective dose (ED50) of naloxone required to precipitate withdrawal jumping responses. The increase in naloxone ED50 was much more pronounced when naltrexone was given prior to and during the course of pellet implantation. Inhibition was also observed when naltrexone was administered 1 day after the morphine pellet implantation. Naltrexone administration prior to and during the development of dependence also partially inhibited the loss in body weight and hypothermic response observed during abrupt withdrawal of morphine in morphine dependent mice. The inhibitory effect of naltrexone on morphine dependence development was not associated with changes in brain morphine concentration. 26 references. (Author abstract modified)

003171 Bigler, E. D.; Shearer, D. E.; Dustman, R. E.; Fleming, D. E. Adolescent Center, Austin State Hospital, 4110 Guadalupe, Austin, TX 78751 **Differential effects of convulsants on visually evoked responses in the albino rat.** Pharmacology Biochemistry and Behavior. 8(6):727-733, 1978.

Visually evoked responses (VER) were recorded from primary visual cortex in unanesthetized rats to study the effects of pharmacological modulation by one of the following convulsant agents: physostigmine, picrotoxin, strychnine, and metrazol. The rat VER consists of six distinct waves constituted by three positive peaks (P1, P2, P3) and three negative peaks (N1, N2, N3). Results indicate a differential convulsant action on VER components. The administration of picrotoxin resulted in a suppression of the peak amplitude of P1-N1 and delayed peak latencies of all components. Strychnine shortened P1, N1, and P2 peak latencies, significantly increased N3 peak latency, and only suppressed P3-N3 amplitude. Physostigmine essentially suppressed all component amplitudes but only increased peak latencies for P2 and P3 components. Metrazol was found to be relatively ineffective in the alteration of any VER component in a systematic manner. The data are discussed in terms of differential modes of convulsant action on the visual system. Implications for convulsant modulation of photically evoked after discharges are considered, and suggestions for further research are offered. 40 references. (Author abstract modified)

003172 Biswas, Bratati; Carlsson, Arvid. Department of Pharmacology, University of Goteborg, Fack, S-40033 Goteborg, Sweden **Effect of intraperitoneally administered GABA on the locomotor activity of mice.** Psychopharmacology (Berlin). 59(1):91-94, 1978.

The effect of intraperitoneal administration of gamma-aminobutyric acid (GABA) at doses from 25-2000mg/kg on spontaneous locomotor activity was examined in female NMRI strain mice. A slight but significant decrease in the spontaneous locomotor activity was seen only with the highest dose. The stimulation of motor activity induced by ethanol (2.4g/kg) was significantly counteracted by GABA (100mg/kg and higher). A further suppression of ethanol-induced hyperactivity was reached by pretreatment with aminooxyacetic acid (15mg/kg). The stimulation of motor activity induced by morphine (10mg/kg) remained unaffected by all doses of GABA. Motility produced by activation of postsynaptic catecholamine receptors through use of: apomorphine (3mg/kg) and clonidine (3mg/kg) following reserpine (10mg/kg) and alpha-methyltyrosine (250mg/kg) pretreatment, was not affected by GABA. GABA enhanced hypomotility caused by a low dose of haloperidol (150microg/kg). Results suggest that blood born GABA can act in the CNS to inhibit the dopaminergic neurons involved in motility regulation. 20 references. (Author abstract modified)

003173 Bloss, James L.; Singer, Garry H. Searle Laboratories, P.O. Box 5110, Chicago, IL 60680 **Neuropharmacological and behavioral evaluation of prostaglandin E2 and 11-thiol-11-desoxy prostaglandin E2 in the mouse and rat.** Psychopharmacology. 57(3):295-302, 1978.

Prostaglandin E2 (PGE2) and 11-thiol-11-desoxy prostaglandin E2 (SHPGE2) were evaluated in mice and rats using a variety of behavioral and neuropharmacological procedures that are sensitive to neuroleptics. Clozapine (C), thioridazine (T), haloperidol (H), and fluphenazine (F) were tested for comparison. All agents except T suppressed avoidance responses in trained rats at one or more doses without concurrently disrupting escape behavior. T, H, and F antagonized lesioned rat rotational behavior at nontoxic doses. T, H, and F induced catalepsy at doses considerably higher than those effective on rotational behavior. SHPGE2, PGE2, and C did not cause catalepsy and did not show statistically significant dose related antagonism of rotational behavior at less than toxic doses. All agents blocked d-amphetamine-induced lethality and caused motor incoordination. SHPGE2, PGE2, C, and T caused statistically significant blockade of physostigmine-induced lethality. It is concluded that SHPGE2 and PGE2 show a spectrum of neuroleptic properties remarkably similar to C. 34 references. (Author abstract)

003174 Bohus, Bela; Kovacs, Gabor L.; DeWied, David. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Utrecht, The Netherlands **Oxytocin, vasopressin and memory: opposite effects on consolidation and retrieval processes.** Brain Research (Amsterdam). 157(2):414-417, 1978.

The effects of intracerebroventricular administration of oxytocin or arginine vasopressin (AVP) on the retention of a passive avoidance response were investigated in male SPF Wistar rats. Administration of oxytocin resulted in an attenuation of the passive avoidance response; the latencies to reenter a former shock compartment were significantly lower than in controls when oxytocin was administered 0, 3, or 23 hours after the learning trial and were not affected when the drug was administered 6 hours after learning. In contrast, AVP facilitated passive avoidance behavior and was most effective when administered 0 or 23 hours after the learning trial. It is concluded that oxytocin attenuates both consolidation and retrieval, while AVP facilitates these processes. 24 references.

003175 Borison, Richard L.; Diamond, Bruce I. Illinois State Psychiatric Institute, Chicago, IL **A new animal model for schizophrenia: interactions with adrenergic mechanisms.** Biological Psychiatry. 13(2):217-225, 1978.

Amphetamine-induced stereotyped behavior in animals is proposed as a model for schizophrenia. Comparison of amphet-

amine-induced stereotype with phenylethylamine (PEA)-induced stereotypy indicates that the alpha-adrenergic blocking agents phentolamine and phenoxybenzamine selectively antagonize PEA-induced stereotypy, whereas the beta-adrenergic blocking agent propranolol fails to alter significantly stereotypies evoked by PEA or amphetamine administration. Catecholamine depletion by alpha-methyl-p-tryosine administration blocks stereotypies induced by both PEA and amphetamine, whereas selective norepinephrine depletion antagonizes only PEA stereotypy. Therefore, PEA elicited stereotypy, but not amphetamine elicited stereotypy, is dependent upon norepinephrine. The significance of this for the PEA animal model of schizophrenia is discussed. 28 references. (Author abstract modified)

003176 Bowden, Nigel J.; Brain, Paul F. Zoology Department, University College of Swansea, Singleton Park, Swansea, SA2 8PP, England **Blockade of testosterone-maintained intermale fighting in albino laboratory mice by an aromatization inhibitor.** Physiology & Behavior. 20(5):543-546, 1978.

The effects of an aromatization inhibitor, 4-androsten-3,6,17-trione (AA), on testosterone and estradiol maintained fighting in castrated male mice were examined. Castrated aggressive Tuck TO strain mice were injected for 17 days with either 25mg testosterone or 4mg estradiol-17beta; 25, 100, or 250mc of AA were also given. Testosterone mediated fighting was effectively blocked by the two higher doses of AA, but estradiol mediated fighting was not. AA alone did nto significantly alter behavior or weights of sex accessory glands. Results suggest that testosterone may be converted to estrogenic metabolites before it has a substantial motivational action on fighting in this species. 14 references. (Author abstract modified)

003177 Brotherton, C. S.; Doggett, N. S. Department of Applied Pharmacology, Welsh School of Pharmacy, University of Wales Institute of Science and Technology, Cardiff, Wales **Modification of the 5-hydroxytryptophan-induced head-twitch response by exogenous endocrine agents.** Psychopharmacology (Berlin). 58(2):145-151, 1978.

Estrogens alone or in combination with progestagens, gonadotrophins, gonadotrophin releasing factor, corticosteroids, and corticotrophin antagonized the head twitch response produced by 5-hydroxytryptophan in female albino mice. In contrast, thryoid hormones, thyrotrophin, and thyrotrophin releasing hormone potentiated the head twitch response. Pretreatment with androgens had no significant effect. Possible mechanisms for these 5-hydroxytryptamine (5-HT) hormone interactions are discussed, including the existence of links between endocrine imbalance and psychological malfunction, which may involve 5-HT as a common denominator. 31 references. (Author abstract modified)

003178 Brown, Z. W.; Amit, Z.; Smith, B.; Rockman, G. E. Center for Research on Drug Dependence, Department of Psychology, Concordia University, Montreal, Quebec, Canada **Differential effects on conditioned taste aversion learning with peripherally and centrally administered acetaldehyde.** Neuropharmacology (Oxford). 17(11):931-935, 1978.

The effects of peripherally and centrally administered acetaldehyde on conditioned taste aversion were investigated in male Wistar rats. The animals were able to learn to associate a novel tasting saccharin solution with the toxic effects of an intraperitoneal injection of acetaldehyde, but no manifestation of a conditioned avoidance of the saccharin taste was evident when the acetaldehyde was administered intracerebroventricularly. It is suggested that the aversive effects of acetaldehyde are mediated by peripheral toxicosis rather than by pharmacological actions of acetaldehyde in the brain. 33 references. (Author abstract modified)

003179 Browne, R. G.; Fondren, B. Department of Psychiatry, School of Medicine, University of California, La Jolla, CA 92093 **Beta-endorphin and the narcotic cue.** Psychopharmacology (Berlin). 58(2):3, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of narcotic cuing properties and beta-endorphin was reported. Male Wistar rats were trained to discriminate either 2.5mg/kg morphine or 2.5ug/kg etonitazene from saline in a two lever operant task for water reinforcement. Following acquisition of these discriminations, the rats were tested for stimulus generalization following various doses and times after subcutaneous injections of morphine, methadone, etonitazene, or D-Methionine2Proline5-enkephalinamide (DMPE). Dose and time dependent generalizations were produced by all three opiates but not by DMPE. The cuing properties of the training drugs were completely antagonized by naloxone. Results of experiments with intraventricularly administered opioid peptides suggest that the opioid peptides produce effects similar to the opiates. The possibility that the cuing properties of opiates are mediated through their actions on endogenous opioid systems is discussed. (Author abstract modified)

003180 Browning, R. A.; Maynert, E. W. Southern Illinois University, School of Medicine, Carbondale, IL 62901 **Effects of intraventricularly administered monoamines on seizure susceptibility and body temperature in rats.** Neuropharmacology (Oxford). 17(8):649-653, 1978.

Male Sprague-Dawley rats injected through intraventricular cannulas with 8mcg norepinephrine, 32mcg dopamine, or 8mcg serotonin were tested 5 minutes later for electroshock seizure threshold and duration of various components of tonic/clonic seizures induced electrically or with flurothyl. Each of the monoamines decreased the threshold for the minimal seizure and increased the duration of the tonic extension and postictal depression phases of maximal electroshock convulsions. Decreased latencies for the myoclonic jerk and generalized convulsions and prolonged recovery from the seizure were observed with flurothyl. All the monoamines produced hypothermia. In animals supplied with sufficient external heat to prevent hypothermia, the decreased electroshock seizure threshold was returned to normal. These findings indicate that the seizure facilitating effects of intraventricularly administered monoamines are attributable to decreased body temperature. 21 references. (Author abstract modified)

003181 Buggy, James; Johnson, Alan Kim. Department of Physiology and Pharmacology, School of Medicine, University of South Carolina, Columbia, SC 29208 **Angiotensin-induced thirst: effects of third ventricle obstruction and periventricular ablation.** Brain Research (Amsterdam). 149(1):117-128, 1978.

The role of periventricular tissue surrounding the anteroventral third ventricle (AV3V) in mediating drinking behavior induced by angiotensin-II was investigated in male Sprague-Dawley rats. Electrolytic lesions which bilaterally destroyed preoptic/hypothalamic tissue surrounding AV3V abolished drinking responses normally elicited by intracerebral injections of angiotensin. In a second experiment, drinking normally induced by lateral preoptic injections of angiotensin was no longer observed when ventricular obstruction prevented drug distribution via cerebrospinal fluid circulation to AV3V periventricular tissue; however, drinking induced by subcutaneous injection of angiotensin was enhanced after ventricular obstruction. Results suggest that centrally or peripherally administered

angiotensin acts on AV3V periventricular tissue to arouse drinking. In contrast to centrally injected angiotensin, peripherally administered angiotensin does not contact receptors by entry and spread in cerebrospinal fluid, but may contact sensitive AV3V tissue directly from blood. 30 references. (Author abstract modified)

003182 Carlson, Kristin R.; Almasi, John. Department of Pharmacology, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01605 **Sensitivity to apomorphine in the guinea pig as a function of age and body weight.** Psychopharmacology. 57(3):279-282, 1978.

Male albino guinea pigs aged 4 to 10 weeks were challenged with 0.1, 0.2, and 0.4mg/kg apomorphine in an attempt to assess the effect of age and bodyweight on changes in apomorphine elicited stereotypies. Mean stereotypy scores rose significantly as a function of age. Stereotypy scores were better correlated with age than with bodyweight, suggesting that CNS maturation rather than weight related factors was responsible. Although age and body weight were correlated, there was enough variability to make body weight an unreliable indicator of age. 19 references. (Author abstract)

003183 Carlson, Kristin R.; Almasi, John. Department of Pharmacology, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01605 **Behavioral supersensitivity to apomorphine following chronic narcotic treatment in the guinea pig.** Psychopharmacology (Berlin). 57(3):273-277, 1978.

Male albino guinea pigs were treated for 3 weeks with methadone, morphine, haloperidol, or saline. One week and 5 weeks following termination of treatment, the animals were challenged with th dopaminergic agonist apomorphine. At the week 1 test, the haloperidol and saline groups did not differ, but behavioral supersensitivity was apparent in significantly elevated mean stereotypy scores of the methadone and morphine groups relative to the saline group; the source of differences in mean scores was a higher peak score rather than increased duration of action. At the week 5 test, the scores of the methadone group were even higher, the morphine group's scores were equivalent to the saline group's, and the haloperidol group's scores were significantly depressed. Results indicate that a 3-week treatment period with methadone or morphine is sufficient to induce dopaminergic supersensitivity and suggest that there may be different time courses for the retention or expression of supersensitivity following these narcotics. 30 references. (Author abstract modified)

003184 Castellano, Claudio. Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R. via Reno, I-00198 Rome, Italy **Effects of mescaline and psilocin on acquisition, consolidation, and performance of light-dark discrimination in two inbred strains of mice.** Psychopharmacology (Berlin). 59(2):129-137, 1978.

The effects of mescaline and psilocin on acquisition, consolidation, and performance of light/dark discrimination were investigated in inbred DBA/2J and C57Bl/6J mice. Pretrial administration of mescaline or psilocin improved the innate tendency of both strains to swim toward a light source in a Y-water maze. The acquisition of a new pattern of behavior (swimming toward the dark arm of the maze) was improved by the hallucinogens in the C57 mice and impaired in the DBA mice. Opposite effects in the two strains (improvement for C57 mice and impairment for the DBA strain) were also observed when either hallucinogen was injected immediately after each training session. Administration of psilocin to mice previously trained to swim toward the dark resulted in performance disruptions in DBA mice but did not effect the C57 strain. 43 references. (Author abstract modified)

003185 Chait, L. d.; Balster, Robert L. Department of Pharmacology, University of rkansas for MEDICAL Sciences, Little Rock, AR 72201 **Interaction between phencyclidine and pentobarbital in several species of laboratory animals.** Communications in Psychopharmacology. 2(4):351-356, 1978.

The interaction of phencyclidine (PCP) and pentobarbital (PB) was investigated in male Swiss-Webster mice, rhesus monkeys, and squirrel monkeys. In mice, 3.0and 30.0mg/kg intraperitoneal PCP significantly lowered the median lethal dose of intraperitoneal PB from a control value of 110mg/kg to 80 and 53mg/kg, respectively. In rhesus monkeys, an inactive dose of PCP (0.20mg/kg intramuscularly) in combination with only a moderate depressant dose of PB (25.0mg/kg intramuscularly) produced surgical anesthesia of over 1 hour duration. In squirrel monkeys, 0.16mg/kg intramuscular PCP failed to enhance the behavioral depressant effect of 12.5mg/kg intramuscular PB; these doses in combination showed a synergistic effect in rhesus monkeys. Results indicate that nondepressant doses of PCP enhance the depressant activity of PB in mouse and rhesus monkey, while squirrel monkeys are insensitive to this enhancement. 13 references. (Author abstract modified)

003186 Cheal, Marylou. Neuropsychology Laboratory, McLean Hospital, Belmont, MA 02178 **Amphetamine effects on stimulus-elicited investigation in the Mongolian gerbil.** Physiology & Behavior. 21(3):299-305, 1978.

The effects of amphetamine on stimulus elicited investigatory behaviors were investigated in Mongolian gerbils. Administration of low acute (0.5-2.0mg/kg) or chronic (0.5-3.0mg/kg) doses of d-amphetamine or sodium chloride had no effect on normal investigation and habituation to a novel object. An acute dose of 3.0mg/kg d-amphetamine significantly attenuated investigatory behavior. Chronic injections of 3.0mg/kg d-amphetamine resulted in less attenuation of investigation, indicating the development of drug tolerance. Single injections of the same doses of amphetamine attenuated investigation of a socially relevant odor, but chronic injections caused a nonlinear attenuation of investigation of the odor. It is concluded that, in the gerbil, amphetamine does not cause increased responsiveness to external stimuli or interfere with habituation; in fact, gerbils respond selectively to specific stimuli in spite of the competition of amphetamine-induced stereotypes with stimulus elicited investigation. 32 references. (Author abstract modified)

003187 Chipkin, R. E.; Stewart, J. M. Department of Biochemistry, University of Colorado Medical Center, Denver, CO 80262 **Potential roles of endogenous peptides in the discriminative properties of drugs.** Psychopharmacology (Berlin). 58(2):4, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, the role of endogenous peptides in the discriminative properties of drugs was discussed. Endogenous peptides can act as agonists relative to exogenously administered agents and as antagonists to other drugs. Peptides may also naturally act as cues for certain adaptive behaviors that have been previously learned. The possible role of adrenocorticotropic hormone as an endogenous stimulus for aggression or escape was considered. 1 reference. (Author abstract modified)

003188 Chipkin, Richard E.; Rosecrans, John A. Department of Psychiatry, Box C-268, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver, CO 80262 **Aversiveness of oral methadone in rats.** Psychopharmacology. 57(3):303-310, 1978.

Palatability gradients were determined between quinine sulfate (0.08mg/ml) and methadone hydrochloride (0.0625, 0.125, and 0.250mg/ml) in naltrexone (3mg/kg/day) and saline treated

male Sprague-Dawley rats presented continuously with these solutions as their only drinking fluids. Saline and naltrexone treated rats chose quinine over the high dose of methadone and the low dose of methadone over quinine. In saline treated animals, consumption of morphine declined by day 7, while naltrexone treated animals showed no change in relative fluid intake or quinine or 0.125mg/ml methadone. Preexposure to methadone solutions as the only drinking fluid available for 7 days prior to presentation of quinine and 0.125mg/ml methadone did not alter the aversive effect of methadone, but the effect was substantially reduced in rats made dependent on morphine immediately before being exposed to the choice solutions. 25 references. (Author abstract modified)

003189 Cole, Sherwood O. Department of Psychology, Rutgers University, Camden, NJ 08102 **Brain mechanisms of amphetamine-induced anorexia, locomotion, and stereotypy: a review.** Neuroscience and Biobehavioral Reviews. 2(2):89-100, 1978.

Evidence on the central mechanisms mediating amphetamine-induced anorexia, locomotion, and stereotypy is reviewed. The central mediation of amphetamine's anorexic effect involves both dopaminergic (nigrostriatal system) and noradrenergic (lateral hypothalamus and ascending noradrenergic pathways) processes, with amygdala-hypothalamic connections and cortical sites serving a possible additional role in such an effect of the drug. The central mediation of amphetamine's locomotor stimulating effect involves both dopaminergic (nigrostriatal and mesolimbic systems) and noradrenergic (ascending noradrenergic pathways as well as their hypothalamic and cortical projections) processes. While the role of amygdala sites in amphetamine-induced locomotion is unclear, additional central processes exert inhibitory influences on the mediation of such an effect of the drug. The central mediation of amphetamine's stereotypical effect involves an exclusive role of the dopaminergic nigrostriatal system, although such mediational principles are influenced by additional inhibitory processes. Finally, evidence on the overlap and dissociation of central processes associated with these behavioral effects of the drug is discussed and the importance of such principles to amphetamine studies briefly indicated. 127 references. (Author abstract)

003190 Colpaert, F. C. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Discriminative stimulus properties of narcotic analgesic drugs.** Psychopharmacology (Berlin). 58(2):4, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, the discriminative stimulus properties of narcotic drugs were reviewed. Available evidence suggests that the narcotic cue is adequately defined as the discriminative stimulus complex that is exclusively associated with the specific central actions of narcotic analgesic drugs. The narcotic cue in rats can serve as a model for opiate-like subjective effects in humans. Neither dopamine, noradrenaline, nor serotonin plays a unique role in the neurotransmitter process underlying the narcotic cue. Other issues discussed include the role of training dose in quantitative and qualitative aspects of the narcotic cue, the possibility that tolerance develops to the physiological drug effects underlying the narcotic cue, the relation between the narcotic cue and the analgesic action of narcotics, the involvement of neurohypophyseal principles in the narcotic cue, the narcotic cue and narcotic state, and the stimulus generalization of endogenous opiate-like substances such as beta-endorphin with the narcotic cue. (Author abstract modified)

003191 Colpaert, F. C.; Niemegeers, C. J. E.; Janssen, P. A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Discriminative stimulus properties of cocaine and d-mphetamine; and antagonism by haloperidol: a comparative study.** Neuropharmacology (Oxford). 17(11):937-942, 1978.

The discriminative stimulus properties of cocaine and diamphetamine and their antagonism by haloperidol were investigated in male Wistar rats. Rates were trained to discriminate 10mg/kg cocaine from saline or 1.25mg/kg d-amphetamine from saline in a discrete trial, two lever, food reward discrimination procedure. Following training, stimulus generalization gradients were determined for cocaine and d-amphetamine in both groups. The acquisition of discrimination proceeded at a comparable rate in the two groups. In both groups, d-amphetamine was about five times more potent that cocaine, and individual threshold doses for the two drugs showed a significant correlation. Haloperidol appeared to be equally effective in antagonizing 1.25mg/kg d-amphetamine and 10mg/kg cocaine. These findings suggest that the cueing properties of d-amphetamine and cocaine are similar. 15 references. (Author abstract modified)

003192 Colpaert, Francis C.; Niemegeers, Carlos J. E.; Janssen, Paul A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Narcotic cuing and analgesic activity of narcotic analgesics: associative and dissociative characteristics.** Psychopharmacology (Berlin). 57(1):21-26, 1978.

By using a discrete trial, two lever, food reinforced discrimination learning paradigm, rats were trained to discriminate the narcotic analgesic fentanyl (0.04mg/kg) from saline. Stimulus generalization experiments with lower fentanyl doses (0.0025 to 0.02mg/kg) were carried out to generate individual threshold doses. These thresholds could not be correlated with the sensitivity of the same rats to the analgesic effect of fentanyl. In a time effect experiment, the duration of fentanyl's cuing effect was compared with that of its analgesic effect, and it was found that the time effect characteristics of the narcotic cue are similar to those of analgesia. Again, however, there was no correlation between the duration of both effects within the same group of animals. 16 references. (Author abstract modified)

003193 Colpaert, Francis C.; Niemegeers, Carlos J. E.; Janssen, Paul A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Neuroleptic interference with the cocaine cue: internal stimulus control of behavior and psychosis.** Psychopharmacology (Berlin). 58(3):247-255, 1978.

The ability of cocaine to exert internal stimulus control of behavior was investigated by training male Wistar rats to discriminate 10mg/kg cocaine from saline in a discrete trial, two choice, food reward procedure. Acquisition of response control by cocaine succeeded in all animals tested, proceeded rapidly, and was associated with a high commission error/omission error ratio. These results support the hypothesis that cocaine, a prototype of drugs inducing a psychotic condition in humans, can act as a powerful internal stimulus in rats. The cocaine cue was also responsive to the action of the dopamine receptor blocking agents spiperone (0.06mg/kg), haloperidol (0.24mg/kg), and pimozide (1.90mg/kg). Administration of d,l-amphetamine (1.25mg/kg) induced stimulus generalization with cocaine, which could be blocked by neuroleptic drugs. Results are discussed in terms of internal stimulus control of behavior and its relevance to the psychophysiology of schizophrenia. 34 references. (Author abstract modified)

003194 Colpaert, Francis C.; Niemegeers, Carlos J. E.; Janssen, Paul A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Changes of sensitivity to the cuing properties of narcotic drugs as evidenced by**

generalization and cross-generalization experiments. Psychopharmacology (Berlin). 58(3):257-262, 1978.

Male Wistar rats were trained to discriminate 0.04mg/kg fentanyl from saline, using a discrete trial, food reward, two lever procedure. Individual threshold doses for generalization of fentanyl and for cross generalization of morphine were determined repeatedly during a 17 week posttraining period. Threshold doses of both drugs shifted almost continuously, both upward and downward. These shifts can best be described by a sustained oscillation, the mean amplitude of which amounts to a factor of 3.65 of the dose range for fentanyl and to a factor of 1.85 for morphine. The upper and lower limits of oscillation were symmetrical with respect to baseline. The oscillation can be described by a function indicating that the more distant a point along the function is from the baseline, the more it is susceptible to positive and negative acceleration along the dose intensity axis. 6 references. (Author abstract modified)

003195 Colpaert, Francis C.; Niemegeers, Carlos J. E.; Janssen, Paul A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Nociceptive stimulation prevents development of tolerance to narcotic analgesia.** European Journal of Pharmacology (Amsterdam). 49(3):335-336, 1978.

The possibility that tolerance to narcotic analgesia does not occur if repeated narcotic administration is accompanied by an adequate level of nociceptive stimulation was investigated in Wistar rats. Animals were divided into four groups: fentanyl (0.04mg/kg twice daily for 4 days); saline (same injection schedule); fentanyl plus exposure to nociceptive stimulation via a crocodile clip applied to hindpaws (fentanyl plus clip); and saline plus clip. Subsequent analgesic tests with 0.04mg/kg fentanyl indicated that the mean analgesic effect in the fentanyl group amounted to about one third of that in the saline group. In contrast, the analgesic effect in the fentanyl plus clip group was similar to that of the saline group and significantly exceeded that in the fentanyl group. These results indicate that tolerance to narcotic analgesia may not occur if repeated drug administration is accompanied by adequate nociceptive stimulation. Findings are discussed in relation to the signal detection theory and to a hypothetical model of the narcotic cue generated by drug discrimination studies. 5 references.

003196 Concannon, J. T.; Smith, G. J.; Spear, N. E.; Scobie, S. R. Department of Psychology, Kent State University, Kent, OH 44242 **Drug cues, drug states, and infantile amnesia.** Psychopharmacology (Berlin). 58(2):4, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the effects of drug cues and drug states on infantile amnesia was reported. Immature rats were conditioned and tested in a drug state to examine the possibility that a drug/drug treatment would improve normally poor retention in young rats and depress normally good retention in more mature rats. In 16-day-old rats, 24 hour retention of fear was state dependent, with the pentobarbital/pentobarbital group excelling all other state dependent comparison groups. In 23-day-old-animals, 24 hour retention was better in the normal/normal condition than in the drug/drug condition. Amphetamine/amphetamine treatment facilitated retention in 11-day-old animals and depressed retention in 13-day-old animals. Findings suggest that drug/drug manipulation facilitates retention only in animals who show rapid normal forgetting and that the drugs act on some postconditioning rehearsal and retrieval process. (Author abstract modified)

003197 Cools, Alexander R.; Wiegant, Victor M.; Gispen, Willem Hendrik. Department of Pharmacology, University of Nijmegan, The Netherlands **Distinct dopaminergic systems in ACTH-induced grooming.** European Journal of Pharmacology (Amsterdam). 50(3):265-268, 1978.

The dopaminergic component in adrenocorticotropic hormone (ACTH) induced excessive grooming was studied. Intraventricular injection of the adrenocorticotropic hormone fragment ACTH1-24 induced excessive grooming behavior in male Wistar rats. This behavior was inhibited by selective pharmacologic manipulation of two functionally distinct types of dopaminergic terminals in the neostriatum or the nucleus accumbens. It is concluded that ACTH1-24 produces excessive grooming by modulating the activity of both inhibitory and excitatory dopaminergic systems. 9 references. (Author abstract modified)

003198 Cooper, J. R.; Overstreet, D. H.; Zimmer-Hart, C. L. School of Social Science, Flinders University of South Australia, Bedford Park, South Australia 5042, Australia **Conditioning factors influence tolerance development to low but not high doses of morphine.** Psychopharmacology (Berlin). 58(2):5, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, studies of the influence of conditioning factors on the development of tolerance to morphine were reported. Morphine treatment (5 and 10mg/kg free base, subcutaneously) was paired with vibrational and photic stimuli, while saline treatment was paired with the absence of these stimuli. A large analgesic response (increased reaction time on a hotplate) was observed after the acute dose of morphine, but tolerance developed rapidly. A small analgesic response to morphine was observed during the probe trial, when the stimuli previously associated with saline administration were paired with the morphine injection. Despite the development of tolerance to morphine for reaction time, no development of tolerance to morphine's suppression of defecation, squealing, or jumping was observed. Tolerance development to the hypothermic effects of morphine was observed, but no influence of conditioning factors could be found. Results generally support the hypothesis that conditioning factors can influence the development of tolerance to morphine, particularly in the case of small doses of morphine. (Author abstract modified)

003199 Cooper, Steven J.; Crummy, Yvonne M. T. Department of Psychology, Queen's University of Belfast, Belfast, BT7 1NN, Northern Ireland **Enhanced choice of familiar food in a food preference test after chlordiazepoxide administration.** Psychopharmacology (Berlin). 59(1):51-56, 1978.

In male Sprague-Dawley rats, chlordiazepoxide (5.0and 10.0mg/kg) increased the time spent eating familiar laboratory chow in a food choice test in which both familiar and novel foods were available. Chlordiazepoxide did not affect the feeding response to the novel food. Prior handling of the rats and repeat testing affected feeding responses in the test, but in ways different from and independent of the effect of chlordiazepoxide. It is concluded that chlordiazepoxide may facilitate feeding responses by direct enhancement of feeding motivation and by either a release of suppression of feeding or an attenuation of anxiety evoked by unfamiliarity. 19 references. (Author abstract modified)

003200 Crossman, A. R.; Sambrook, M. A. Department of Anatomy, Medical School, University of Manchester, Manchester M13 9PT, England **The neurological basis of motor asymmetry following unilateral nigrostriatal lesions in the rat: the effect of secondary superior colliculus lesions.** Brain Research (Amsterdam). 159(1):211-213, 1978.

The effect of bilateral lesions of the superior colliculus on drug-induced turning behavior was investigated in female Sprague-Dawley rats previously given unilateral 6-hydroxydopamine

(6-OHDA) nigrostriatal lesions. The collicular lesions did not significantly effect turning induced by either apomorphine or amphetamine. Results indicate that the integrity of the superior colliculi and the tectospinal tracts is not required for the maintenance of rotational movement following unilateral 6-OHDA nigrostriatal lesions. It is suggested that the role of the striatum in rotational movements may be mediated by apparently minor projections from the pallidum or substantia nigra to the brainstem tegmentum. 5 references.

003201 Cummins, R. A.; Carlyon, T. N.; Walsh, R. N. Department of Psychology, University of Western Australia, Australia **Drug-modulated behavioural responses to environmental enrichment.** Psychopharmacology (Berlin). 58(2):197-199, 1978.

The effects of strychnine and chlorpromazine (CPZ) on behavioral responses to environmental enrichment were assessed in male Quackenbush mice. The mice were given daily injections of strychnine (0.5mg/kg), CPZ (6.0mg/kg), or saline, and were housed in either social or enriched sensory environments. Both CPZ and social rearing depressed home cage activity. Strychnine also depressed activity, but only in the social group. Findings support earlier works on the subject. 9 references. (Author abstract modified)

003202 D'Mello, G. D.; Stolerman, I. P. MRC Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **Methodological issues in drug-discrimination research.** Psychopharmacology (Berlin). 58(2):5, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a comparative study of a two bar operant procedure (spatial task) and tasks involving audiovisual or flavor cues was reported. Rats were trained to drink for food reward delivered on a tandem variable interval 1' fixed ratio 20 schedule. Two drinking tubes were then presented simultaneously and the correct tube was indicated by amphetamine or saline injection. The use of drinking rather than barpressing made little difference in acquisition of spatial tasks. Conventional, spatial stimuli were more effective than either flavor or audiovisual stimuli in determining response choice. Additional studies with morphine, amphetamine, and cocaine emphasized the importance of complete crossover designs in combination with dose response determinations in making valid comparisons of drugs by means of the discriminative stimuli which they produce. (Author abstract modified)

003203 Davies, J. A.; Williams, J. Department of Pharmacology, Welsh National School of Medicine, Heath Park, Cardiff, Wales **The effect of baclofen on alpha-flupenthixol-induced catalepsy in the rat.** British Journal of Pharmacology (London). 62(2):303-305, 1978.

The effect of baclofen (beta-p-chlorophenyl-gamma-aminobutyric acid) on the cataleptogenic effect of alpha-flupenthixol (a-FPT) was examined. The a-FPT, 0.2mg/kg i.p.,produced catalepsy in rats. Baclofen (10mg/kg i.p.)given 30 min after a-FPT had a biphasic effect on the catalepsy. Initially there was a potentiation of the effect, followed by a significant attenuation of the degree of catalepsy. Possible mechanisms of action, involving dopaminergic systems in the nigrostriatum, are discussed. 12 references. (Author abstract modified)

003204 Davis, Hasker P.; Rosenzweig, Mark R.; Bennett, Edward L.; Orme, Ann E. Department of Psychology, University of California, Berkeley, CA 94720 **Recovery as a function of the degree of amnesia due to protein synthesis inhibition.** Pharmacology Biochemistry and Behavior. 8(6):701-710, 1978.

Two theories explaining recovery from retrograde amnesia produced by protein synthesis inhibition are examined. A controversy centers around whether the induced retention deficit reflects a failure to consolidate memory or whether it reflects an impairment in the retrieval process. Major evidence for the retrieval hypothesis is provided by studies utilizing a reminder (usually footshock) to attenuate the effect of the protein inhibitor. To examine this question, mice were injected subcutaneously with anisomycin and given one training trial in a passive avoidance box. All animals received a single retention test on each of four consecutive dates, starting either 1, 7, or 21 days after training. One half the mice in each group received a footshock reminder one hour after their initial test. The reminder did not attenuate the inhibitor-induced amnesia, but multiple testing did produce partial recovery in animals demonstrating some memory of training. Animals injected with anisomycin whose testing began one day after training demonstrated partial recovery irrespective of drug dosage level. The extent of amnesia and recovery were dependent upon both drug dosage and training test interval. Implications for the consolidation and retrieval theories are discussed. 35 references. (Author abstract modified)

003205 Davis, Joel L.; Gerbrandt, Lauren K.; Cherkin, Arthur. Psychobiology Research Laboratory, V.A. Hospital, Sepulveda, CA 91343 **Retroactive amnesia induced in chicks by the proline analog L-baikiain, without EEG seizures or depression.** Physiology & Behavior. 21(4):653-658, 1978.

Chicks were injected intracerebrally with 5mcl/hemisphere of 150mM L-baikiain, L-proline, or D-proline, 1 minute after one trial training to suppress the spontaneous peck response to a stainless steel bead. L-baikiain proved to be an effective retroactive amnestic agent, compared to D-proline controls. The amnestic effect induced by 1.5mcmols of L-baikiain was comparable to that found with 6.0mcmols of L-proline in previous experiments. Electrophysiological recording of multiple unit activity and raw integrated EEG activity showed no seizure spiking or isoelectric activity. No reliable differences in EEG and multiple unit activity were observed between L-baikiain and D-proline injections. It is concluded that L-baikiain is approximately four times more potent than L-proline as an amnestic agent and that both compounds are effective at doses that caused no marked electrophysiological changes. 11 references. (Author abstract modified)

003206 Davis, Stephen F.; Gussetto, John K.; Tramill, James L. Neideffer, Jerry; Travis-Neideffer, Mary Nell. Austin Peay State University, Clarksville, TN 37040 **The effects of extended insulin dosage on target-directed attack and biting elicited by tail-shock.** Bulletin of the Psychonomic Society. 12(1):80-82, 1978.

To further delineate the relationship between low blood sugar level experimentally induced by insulin injection and agggression, two experiments are presented in which rats receive 12, 16, 20, 24, 28, or 32 units of regular zinc insulin prior to shock testing. Response level for the 12 unit insulin group was significantly higher than that for all other groups in both experiments; response level of the 24 unit group was higher than that of the 16 and 20 unit groups. When dosage levels of 12, 28, and 32 units were used to investigate this elevated responding, high and virtually identical response level were shown by the 12 unit and 28 unit groups with an extremely low response level shown by the 32 unit group. Possible explanations of these variations are discussed. 6 references. (Author abstract modified)

003207 de Caro, G.; Massi, M.; Micossi, L. G.; Venturi, F. Institute of Pharmacology and Pharmacognosy, Faculty of Pharmacy, University of Camerino, Italy **Physalaemin, a new potent antidipsogen in the rat.** Neoropharmacology (Oxford). 17(11):925-929, 1978.

The effect of intracerebroventricular administration of the naturally occurring endecapeptide physalaemin on water intake in male Wistar rats was investigated. Drinking was induced by intracerebroventricular injection of 100mg angiotensin II or 300ng carbachol, water deprivation, or sodium chloride load. Physalaemin produced a dose dependent inhibition of water intake induced by angiotensin II or carbachol, with virtually complete inhibition at doses of 500ng and 1mcg, respectively. In water deprived rats, 10mcg, but not lower doses, of the peptide produced a significant inhibition of water intake. The effect was short lasting and ceased 30 minutes after the injection. Physalaemin was completely ineffective in sodium chloride loaded rats, even in very large doses (up to 5mcg). Although the mechanism of physalaemin's potent antidipsogenic action is not yet known, it appears to be specific to the CNS and not simply due to the marked vascular activity of the peptide. 9 references. (Author abstract modified)

003208 Decsi, Laszlo; Nagy, Julia; Zambo, Katalin. Institute of Pharmacology, University Medical School, H-7643 Pecs, Hungary **Stereotyped behavior after cholinergic, but not dopaminergic, stimulation of the substantia nigra in rats.** Life Sciences. 22(21):1873-1878, 1978.

Stereotyped behavior was measured in Wistar rats after intracerebral application of dopaminergic and cholinergic drugs. Bilateral intranigral injection of apomorphine (APO) did not evoke any signs of stereotyped behavior. Application of APO in the amygdaloid nucleus also failed to cause stereotypy. Dopaminergic blockade of the substantia nigra by topical application of triperidol failed to influence the stereotypy elicited by systemic APO administration. Direct cholinergic stimulation of the substantia nigra with carbachol resulted in dose related stereotyped behavior similar to that evoked by systemic APO. The effect of intranigral carbachol was antagonized by pretreatment with a 10mg/kg intraperitoneal injection of atropine. Stereotypy was also produced by intracaudate application of APO. Topical triperidol blockade of the caudate nucleus prevented the stereotypy caused by intraperitoneal APO. It is concluded that some nigral neurons cannot be directly excited by APO but can be excited by carbachol, which suggests that they contain muscarinic receptors involved in stereotyped behavior. 8 references. (Author abstract modified)

003209 Deutsch, Robert. Department of Psychology, Atkinson College, York University, Downsview, Ontario, M3J 2R7, Canada **Effects of atropine on conditioned taste aversion.** Pharmacology Biochemistry and Behavior. 8(6):685-694, 1978.

Atropine sulfate was used as an anticholinergic drug in several experiments to investigate how manipulation of the cholinergic system in rats influences their conditioned taste aversion. Intraperitoneal injections of atropine sulfate shortly before tasting were found to interfere with conditioning of the aversion, but injection of atropine after tasting did not. The interference effect was also obtained with intraventricular administration of atropine sulfate, but not with intraperitoneal injection of the peripherally acting atropine methylnitrate. These results show that central rather than peripheral mechanisms are involved in this effect, and suggest that conditioned taste aversion, like other kinds of learning, involves cholinergic mediation. 58 references. (Author abstract modified)

003210 Divac, Ivan; Markowitsch, Hans J.; Pritzel, Monika. Institute of Neurophysiology, University of Copenhagen, 36 Juliane Mariesvej, DK-2100 Copenhagen, Denmark **Behavioral and anatomical consenquences of small intrastriatal injections of kainic acid in the rat.** Brain Research (Amsterdam). 151(3):523-532, 1978.

The behavior and anatomical effects of bilateral injections of kainic acid into the anteromedial neostriatal region were examined in male Wistar rats. Kainic acid produced a severe impairment of delayed alternation retention, but did not affect visual discrimination ability. Axons traversing the injected area were able to transport horseradish peroxidase. Histological examination of the injected regions revealed a heavy loss of neurons and a decrease in histochemical straining for specific acetylcholinesterase. Silver impregnation showed slightly disorganized but continuous axons in bundles of the capsula interna. The axonal network throughout the neuropil of the injected area was markedly diminished. No conspicuous change was found in myelin staining or in the intensity of catecholamine fluorescence. The anatomical results suggest that kainic acid affects only perikarya of the neostriatum and axons originating from these perikarya, while passing axons remain intact. The observed behavioral changes must therefore be attributed to changes in the neostriatum itself. It is concluded that the neostriatum has complex or cognitive function and that some ental symptoms in Huntington's chorea may be attributed to a dysfunction in this pat of the brain. 36 references. (Author abstract modified)

003211 Dudek, Bruce C.; Fuller, John L. Dept. of Psychology, State University of New York, Binghamton, NY 13901 **Task-dependent genetic influences on behavioral response of mice (Mus musculus) to acetaldehyde.** Journal of Comparative and Physiological Psychology. 92(4):749-758, 1978.

Acetaldehyde was employed as a pharmacological agent in behavioral tests designed to assess genetic influences upon response to the drug. When used as a poison in a conditioned taste aversion study, acetaldehyde was more effective at inducing aversions in DBA/2J mice than in C57BL/6J mice. In another experiment, however, C57 mice were more affected than were DBA mice by acetaldehyde effects on loss of righting reflex. Implications for postulated genetic control of ethanol preference and neurosensitivity are discussed. 33 references. (Author abstract)

003212 Eastgate, Sheila M.; Wright, James J.; Werry, John S. Department of Psychiatry, School of Medicine, University of Auckland, Auckland, New Zealand **Behavioural effects of methylphenidate in 6-hydroxydopamine-treated neonatal rats.** Psychopharmacology (Berlin). 58(2):157-159, 1978.

The effects of methylphenidate on activity were examined in an animal model of minimal brain dysfunction (MBD) to determine to what extent, if any, the response to central stimulants is impaired. Neonatal Wistar rats treated at 7 days of age with 6-hydroxydopamine showed normal levels of activity during maturation. When these animals were also treated with methylphenidate hydrochloride between 14 and 22 days of age, they showed less hyperactivity than controls. Comparison of these results with those of other workers suggests that several experimental variables must be controlled precisely if reproducible results analogous to the disturbed behavior of children with MBD are to be obtained with this animal model. 20 references. (Author abstract modified)

003213 Eckerman, David A.; Lanson, Robert N.; Berryman, Robert. Dept. of Psychology, University of North Carolina, Chapel Hill, NC 27514 **Effects of sodium pentobarbital on symbolic matching and symbolic oddity performance.** Bulletin of the Psychonomic Society. 11(3):171-174, 1978.

The hypothesis that complex discrimination tasks are more easily disrupted by drugs than are simpler ones was studied by examining the effects of sodium pentobarbital on symbolic matching and symbolic oddity performance by pigeons. Results

show that pigeons' conditional discrimination accuracy was equally disrupted by administering sodium pentobarbital when the discrimination required a three alternative symbolic matching to sample task (if blue, select green; if greeen, select red; if red, select blue) as when it required a three alternative symbolic oddity from sample task (if blue, select anything but green; etc.). This equivalence in disruption makes difficult interpretation of prior findings showing simple matching to sample (if blue, select blue; if green, select green; etc.)to be more disrupted by drugs than was simple oddity (if blue, select anything but blue; etc.). 6 references. (Author abstract modified)

003214 Einon, Dorothy F.; Morgan, Michael J.; Kibbler, Christopher C. Dept. of Psychology, University of Durham, Science Laboratories, South Road, Durham DH1 3LE, England **Brief periods of socialization and later behavior in the rat.** Developmental Psychobiology. 11(3):213-225, 1978.

Juvenile rats were allowed short daily periods of social contact to see if this would reduce the known effects of isolation rearing upon habituation of locomotor activity and object contact in the open field. Subjects were female Lister hooded rats. Animals totally deprivedof social experience (ISOL) were slower to habituate than animals living in small social groups (SOC). Rats allowed 1 hour of social contact (partial isolates, PI), but living otherwise in isolation, were intermediate between ISOL and SOC animals. In further experiments the quality of social interactions in the daily period was altered by drugging one of the partners, either with amphetamine or with chlorpromazine. In later tests in the open field, the rats that had interacted with amphetamine injected or chlorpromazine injected partners differed from PI animals in the direction of resembling complete isolates; [this was particularly true of those paired with amphetamine animals. Observation revealed that injection of one of the partners considerably altered social interactions in the pair. A further test showed that 1 hour of contact a day considerably alleviated the deleterious effects of isolation rearing upon response reversal. It is concluded that normal development in the rat may depend upon the flexibility of behavior encouraged by the early social situation. 22 references. (Author abstract)

003215 Eison, Michael S.; Wilson, W. Jeffrey; Ellison, Gaylord. Department of Psychology, University of California, Los Angeles, CA 90024 **A refillable system for continuous amphetamine administration: effects upon social behavior in rat colonies.** Communications in Psychopharmacology. 2(2):151-157, 1978.

A study of the effects of continuous amphetamine administration upon social behavior in rat colonies was conducted. The continuous presence of the drug was insured by the twice daily filling of a subcutaneous delivery system with more d-amphetamine base than was released during the time between refills. The rats exhibited a three phase behavioral syndrome during 10 days of continuous drug administration. Initially exploratory and hyperactive, they then entered a prolonged stereotypy phase lasting 4 days. A distinct behavioral transition out of stereotypy, followed by exaggerated social behaviors and increased frequency of spontaneous startle responses occurred 6 days after the first loop fill. These data corroborate a previously described behavioral syndrome observed after implantation of a nonrefillable amphetamine pellet in rats, and imply that continuous administration of amphetamine to rats can provide a sueful animal model of amphetamine psychosis. 8 references. (Author abstract modified)

003216 Esposito, Ralph U.; Kornetsky, Conan. Laboratory of Behavioral Pharmacology, Division of Psychiatry, Boston University School of Medicine, 80 E. Concord St., Boston, MA 02118 **Opioids and rewarding brain stimulation.** Neuroscience and Biobehavioral Reviews. 2(2):115-122, 1978.

Studies are reviewed which demonstrate opioid-induced facilitative effects on self-stimulation to a number of different neuroanatomical sites in the rat brain. Tolerance has not been demonstrated to this facilitation. Evidence supports the contention that these behavioral effects reflect an increase in sensitivity of the neuronal pathways subserving brain stimulation reward. It is proposed that these actions are directly related to the hedonic subjective effects and addiction liability associated with human use of opioids. 61 references. (Author abstract)

003217 Feldman, Robert S.; Smith, William C. University of Massachusetts, Amherst, MA 01003 **Chlordiazepoxide-fluoxetine interactions on food intake in free-feeding rats.** Pharmacology Biochemistry and Behavior. 8(6):749-752, 1978.

The effects of chlordiazepoxide (CDP) and fluoxetine (FXT) on food intake in free feeding male Sprague-Dawley abino rats was studied to determine whether this drug inhibits a satiety mechanism, or activates or facilitates a hunger mechanism. CDP, which blocks serotonin turnover, increased food intake in free feeding rats. FXT, a serotonin agonist, decreased food intake. Administration of combinations of the two drugs showed an antagonistic dose dependent relationship, implicating a satiety of hunger mechanism that is mediated by serotonin. 26 references. (Author abstract modified)

003218 File, Sandra E. Dept. of Pharmacology, School of Pharmacology, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Exploration in immature rats: effects of drugs.** Developmental Psychobiology. 11(5):405-412, 1978.

The effects of d-amphetamine (4mg/kg), scopolamine (1mg/kg), methylscopolamine (1mg/kg), and parachlorophenylalanine (400mg/kg) on exploration were studied in male rats at 16, 21, and 28 days of age. Amphetamine elicited stereotypy at all ages, reduced exploration (measured by time spent head dipping during a 10 min trial) from day 21, but did not significantly increase rearing at the ages tested. Scopolamine reduced head dipping at all ages tested, whereas in adults it produced an increase. The age related difference in drug effects suggests that muscarinic pathways are functioning from day 16, but that the system concerned with exploration functions differently in mature and immature rats. Both scopolamine and methylscopolamine reduced rearing, suggesting that the change is due to peripheral actions of the drugs. Parachlorophenylalanine, which decreases serotonin levels, increased head dipping, as it does in adult rats. 20 references. (Author abstract modified)

003219 File, Sandra E.; Hyde, J. R. G. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Can social interaction be used to measure anxiety?** British Journal of Pharmacology (London). 62(1):19-24, 1978.

Changes in social interactions among pairs of male hooded rats and their behavioral correlates were examined under various test conditions and the effects of chronically administered chlordiazepoxide (CDZ) upon social interactions were studied. Maximum active interaction was found when the rats were tested under low light in a box with which they were familiar. Social interaction and exploration decreased when the light level was increased or when the light level was increased or when the box was unfamiliar. As these decreased, defecation and freezing increased. Anosmic controls showed that the decrease in social interaction across test conditions could not be attributed to olfactory changes in the partner. CDZ (5mg/kg) given chronically prevented or significantly reduced the de-

crease in social interaction that occurred in undrugged rats as the light level or unfamiliarity of the test box was increased. Controls showed that this effect could not be entirely attributed to CDZ acting selectively to increase low levels of responding. This effect of CDZ contrasts with its acute effect, which is only sedative. The utility of this test as an animal model of anxiety is discussed. 20 references. (Author abstract modified)

003220 Foreman, Mark M.; Moss, Robert L. Department of Obstetrics and Gynecology, University of Texas Health Science Center at Dallas, Dallas, TX 75235 **Role of hypothalamic serotonergic receptors in the control of lordosis behavior in the female rat.** Hormones and Behavior. 10(1):97-106, 1978.

The role of serotonin (5-hydroxytryptamine, or 5-HT) in mediating hypothalamic control of sexual behavior in estrone primed ovariectomized (OVX) rats was studied by comparing the lordotic patterns followingo medial preoptic (MPOA) and arcuate-ventromedial (ARC-VM) infusions of 5-HT, methysergide (MS), and vehicle. In animals primed with low doses of estrone 48 hours prior to mating, lordotic behavior was significantly enhanced by infusion of MS in the MPOA or ARC-VM, but was not significantly affected by 5-HT infusion. Significant depressions in lordotic behavior were observed, however, following 5-HT infusions in OVX rats primed with higher doses of estrone to maintain a high level of receptivity. The infusion of luteinizing hormone releasing hormone (LRH) into the MPOA or ARC-VM significantly enhanced lordotic behavior in OVX rats primed with low doses of estrone, but the addition of 5-HT to the LRH infusate abolished this behavioral enhancement. It is concluded that serotonergic receptors within the MPOA or ARC-VM areas have inhibitory effects on lordotic behavior, and that LRH and 5-HT have opposing effects within these forebrain areas. 35 references. (Author abstract modified)

003221 Fouriezos, George; Hansson, Peter; Wise, Roy A. Dept. of Psychology, Concordia University, 1455 de Maisonneuve Boulevard West, Montreal, Quebec H3G 1M8, Canada **Neuroleptic-induced attenuation of brain stimulation reward in rats.** Journal of Comparative and Physiological Psychology. 92(4):661-671, 1978.

Neuroleptic induced attenuation of brain stimulation reward in rats was investigated. In 30 min free operant tests, the dopamine receptor blockers pimozide and ()-butaclamol attenuated lever-pressing for lateral hypothalamic brain stimulation. Performance early in both lever pressing and runway sessions was normal; performance deteriorated as testing progressed, following patterns that paralleled those seen when animals were tested with reductions in the amplitude of stimulating current. Data support the view that central dopaminergic systems are important components of the neural mechanisms mediating reward. 39 references. (Author abstract modified)

003222 Francis, N.; Marley, E.; Stephenson, J. D. Department of Pharmacology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, England **Effects of spiperone on self-stimulation and other activities of the Mongolian gerbil.** British Journal of Pharmacology (London). 63(1):43-49, 1978.

The effects of spiperone on self-stimulation obtained with conventional lever-pressing and self-stimulation obtained with a capacitance probe requiring only touch were investigated in Mongolian gerbils. Lever-pressing was more sensitive to the decremental effects of pentobarbitone than capacitance probe touching, suggesting its greater responsiveness to disturbances of motor function. Spiperone (0.005 to 0.05mg/kg) attenuated capacitance probe touching and lever-pressing equally. The same dose range of spiperone was found to attenuate locomotor activity, whether spontaneous or evoked by noncontingent electrical stimulation, and produce catalepsy. The spiperone induced attenuation of self-stimulation was not necessarily a result of its action on dopaminergic reward pathways, since the effects could be explained equally well by a failure to initiate responding. 13 references. (Author abstract modified)

003223 Freeman, Gary B.; Wallace, Robert B.; Werboff, Jack; Graziadei, Robert B.; Root, Mark; Smith, Philip; Warner, Norman W. University of Hartford, West Hartford, CT 06117 **Activity analysis of operant behavior following methylphenidate administration.** Perceptual and Motor Skills. 47(1):163-167, 1978.

Thirteen male Long Evans hooded rats were tested on a CRF 50 reinforcement schedule to determine the effects of methylphenidate administration. Total response time as well as time and total activity responses away from the bar were significantly influenced by injections of methylphenidate. The data supported previous findings of reduced response rate to the drug. However, methylphenidate (a central nervous sytem stimulant) increased activity that was not related to bar-pressing. Analysis of activity response to drug, it is concluded, should include total time and activity as well as operant rates. 10 references. (Author abstract modified)

003224 Freemark, Michael; Stoff, David M.; Moja, Egidio A.; Gillin, J. Christian; Wyatt, Richard J. National Institute of Mental Health, St. Elizabeths Hospital, Washington, D. C. **Testosterone-attenuated stereotypy and hyperactivity induced by beta-phenylethylamine in pargyline-pretreated rats.** Biological Psychiatry. 13(4):455-463, 1978.

The possibility that testosterone might alter the response of immature rats given beta-phenylethylamine was investigated. Testosterone pretreatment attenuated, in a dose response fashion, the induction of stereotyped behavior and hyperactivity by pargyline and beta-phenylethylamine in prepubertal, male rats. The dyskinetic movements induced by pargyline and beta-phenylethylamine were proposed as a possible animal model for tardive dyskinesias. Attenuation by testosterone of these effects suggested an hormonal involvement consistent with the reported predominant occurrence of tardive dyskinesias in women and in the elderly. 32 references. (Author abstract modified)

003225 Frigeni, V.; Bruno, F.; Carenzi, A.; Racagni, G.; Santini, V. Research Laboratories, Bresso-Milan, Italy **Analgesia and motor activity elicited by morphine and enkephalins in two inbred strains of mice.** Journal of Pharmacy and Pharmacology (London). 30(5):310-311, 1978.

The results of intracerebroventricular administration of morphine were compared to those results obtained from: 1) intraperitoneal injections of morphine and 2) injection of methionine (MEt) enkephalin and the more potent Ala2-Met-enkephalin. One hour after injection of morphine a four fold increase in motor activity was evident in C57 BL/J mice in comparison with DBA mice. On the contrary, the analgesic response to morphine in DBA mice was greater than that the analgesic respose to morphine in DBA mice was greater than that obtained in C 57 mice (Fig. 1B). Both responses differ from that obtained in Swiss mice. Met-enkephalin, like morphine, was more potent in eliciting analgesia in DBA than in C57 mice, while no motor response was observed in any of the strains investigated (Fig. 1D and 1C). Similar results were obtained using D-Ala2-Met-enkephalin at the dose ten times higher than the corresponding ED50 for analgesia. It is concluded that genetic mechanisms seem to play an important role when the effects of morphine are assessed on the locomotor and analgesic behavior of mice. 12 references.

003226 Fujiwara, Michihiro; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu

University 62, Fukuoka 812, Japan **Muricide induced by single injection of delta9-tetrahydrocannabinol.** Physiology & Behavior. 21(4):581-585, 1978.

The effects of a single dose of delta9-tetrahydrocannabinol (THC) on the occurrence and course of muricide in isolated male Wistar King A rats were investigated. Dose related muricide was observed 1 hour after THC injection in rats that had been subjected to 22 hours of food deprivation and 24 hours of isolated housing. In a second experiment, muricide appeared in 60-80% of animals given a single dose of THC, regardless of the duration of isolation (2 hours to 30 days) or the time of injection. Muricide was not induced in communally housed rats treated with THC. However, when communally housed rats were placed in isolation 1 hour after treatment, the time of peak effect of THC, muricide occurred in 70% of the animals. Results indicate that muricide is induced in rats placed in isolation within the effective period of THC. 20 references. (Author abstract modified)

003227 Gibbs, Marie E.; Gibbs, Colin L. : Ng, Kim T. Department of Psychology, La Trobe University, Bundoora, Victoria 3083, Australia **A possible physiological mechanism for short-term memory.** Physiology & Behavior. 20(5):619-627, 1978.

The influence of potassium on memory formation was examined in 1-day-old chicks. Memory formation for a passive avoidance task was inhibited by intracranial injections of very low concentrations (1 and 2mM) of potassium chloride (KCl). These effects occurred shortly after learning, in the first of a postulated three phase sequence of memory formation. Concentrations of KCl between 2.5and 5.0mM inhibited the second of the three phase sequence. KCl concentrations lower than 1mM or comparable to normal cerebrospinal fluid levels (7mM) produced no effects on memory. Concentrations of sodium chloride different for normal cerebrospinal fluid concentrations in the young chick produced small but consistent memory deficits; these effects were independent of those due to KCl. It is argued that short-term memory formation involves afferent posttentanic hyperpolarization that is inhibited by potassium accumulation at synapses following glia inactivation. 48 references. (Author abstract)

003228 Glick, Stanley D.; Cox, Russell D. Department of Pharmacology, Mount Sinai School of Medicine, City University of New York, Fifth Avenue and 100th Street, New York, NY 10029 **Changes in morphine self-administration after tel-diencephalic lesions in rats.** Psychopharmacology. 57(3):283-288, 1978.

Rats were trained to barpress for intravenous infusions of morphine sulphate during 1 hour daily test sessions in an attempt to determine the specificity of the caudate influence and its possible modulation by other structures. Rates of morphine self-administration were enhanced by lesions of the frontal cortex and hippocampus and transiently reduced by lesions of the medial forebrain bundle and medial thalamus. Dose response studies indicated that sensitivity to morphine's rewarding property was decreased by frontal cortical and hippocampal lesions. Lesions of the posterior cortex, the tuberculum olfactorium, and the nucleus accumbens had no effect on self-administration behavior. Results are discussed in relation to previous findings with caudate and brainstem lesions, and a neuroanatomical substrate for morphine reinforcement is suggested. 31 references. (Author abstract)

003229 Goas, J. Allen; Lippa, Arnold S. Central Nervous System Disease Research Section, Lederle Laboratories, Pearl River, NY 10965 **Bimodal distributions of highest ethanol acceptance concentrations in two strains of rats.** Pharmacology Biochemistry and Behavior. 8(6):695-699, 1978.

Rats' preference for various ethanol concentrations over water was examined. Two groups of nondeprived male Wistar rats and one group of male Sprague-Dawley rats were offered a choice of water and daily increasing concentrations of ethanol. Each group's distribution of highest ethanol acceptance concentrations approximated a binmodal distribution with respect to concentration. Further, rats in each group which drank ethanol at high concentrations maintained relatively constant intakes of pure ethanol. These results are discussed in terms of taste and olfaction, central nervous system sensitivity and emotionality. 23 references. (Author abstract modified)

003230 Gordon, John H.; Bromley, Bruce L.; Gorski, Roger A.; Zimmermann, E. Department of Anatomy, University of California, Los Angeles, CA 90024 **Delta9-tetrahydrocannabinol enhancement of lordosis behavior in estrogen treated female rats.** Pharmacology Biochemistry and Behavior. 8(5):603-608, 1978.

The effect of delta9-tetrahydrocannabinol (THC) on lordosis behavior was examined in ovariectomized rats. Animals were treated with THC (1.25, 2.50, or 10.00mg/kg/day) or estradiol benzoate (EB, 2.0microg/kg/day) plus THD (10.0mg/kg/day) followed by 500microg progesterone (PROG) for 5 days prior to testing for lordosis behavior. Control animals and animals treated with THC alone failed to show any lordosis behavior, and the behavioral effects of EB were not antagonized by THC. In EB primed rats, low doses (0.5and 1.5mg/kg) of THC significantly enhanced lordosis behavior, while a higher dose (3.0mg/kg) attenuated the response. Following adrenalectomy, the dose response curve for THC was shifted to the left. The THC enhancement of lordosis behavior in EB primed rats could not be attributed to release of PROG from the adrenals. THC appears to enhance sexual receptivity in female rats by a direct action on the CNS. 58 references. (Author abstract modified)

003231 Gotestam, K. G. University of Trondheim, Ostmarka Hospital, Box 3008, N-7001 Trondheim, Norway **Reinforcing, discriminative, and/or activation properties of amphetamine.** Psychopharmacology (Berlin). 58(2):6, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, studies of the reinforcing, discriminative, and activating effects of amphetamine were reported. In rats, self-administration of amphetamine followed by saline substitution resulted in greatly increased saline self-administration, which suggests that amphetamine acted as a discriminative stimulus. In rats trained to press a lever for food following a single amphetamine dose, lever pressing was increased during nonreinforced test sessions. Single doses of amphetamine did not alter food reward response patterns during extinction sessions. Neither saline nor amphetamine altered extinction patterns of food reinforced behavior when followed by a single amphetamine dose. Findings suggest that increased rates of responding during self-administration experiments and during extinction of drug discrimination are not entirely a function of the activating effects of amphetamine. (Author abstract modified)

003232 Goudie, A. J.; Dickins, D. W.; Thornton, E. W. Psychology Department, Liverpool University, Liverpool, L69 3BX, England **Cocaine-induced conditioned taste aversions in rats.** Pharmacology Biochemistry and Behavior. 8(6):757-761, 1978.

Aversion properties of cocaine on conditioned taste in albino rat was examined. In two separate studies cocaine hydrochloride at doses between 10 and 36 mg/kg was found to induce a dose related conditioned taste aversion (CTA) to saccharin, and to be an effective conditioning agent even when injections of the drugs were delayed for 90 minutes after saccharin intake.

Only doses with extensive behavioral effects were effective in conditioning and even high doses were only effective in producing relatively limited suppression of intake. Findings of the second experiment constitute systematic replication of the first results. These data contrast with an earlier report that suggested that cocaine was totally devoid of aversive properties. However, they do indicate that it is only a weak aversion inducing agent. In contrast to other drugs, the doses of cocaine required to induce a CTA are very large relative to those commonly employed in behavioral studies. The weak potency of cocaine in inducing CTA may be related to the drug's marked potency in the self-administration paradigm. Some possible determinants of cocaine's weak effects are discussed. 24 references. (Author abstract modified)

003233 Graeff, F. G.; Arisawa, E. A. L. Department of Pharmacology, School of Medicine, 14.100 Ribeirao Preto, Sao Paulo, Brazil **Effect of intracerebroventricular bradykinin, angiotensin II, and substance P on multiple fixed-interval fixed-ratio responding in rabbits.** Psychopharmacology (Berlin). 57(1):89-95, 1978.

The dose effect relationships of intraventricularly injected bradykinin, angiotensin II, and substance-P on lever lifting behavior of rabbits in a multiple fixed-interval (FI) 2 minute, fixed-ratio (FR) 15 responses schedule of sweetened water presentation were determined. Bradykinin (30mg and 56ng) increased FI response rates and had no effect on FR responding. Angiotensin II (3ng) increased only FR response rates. Higher doses of both peptides caused dose dependent decreases in both FI and FR response rates. Substance-P (0.1, 0.3, and 1.0micrograms) caused dose dependent decreases in FI and FR response rates with no initial pause, while 3.0micrograms of substance-P caused an initial response suppression as well as comparable decreases in FI and FR rates. Results show that small amounts of bradykinin, angiotensin II, and substance-P cause specific and selective effects on operant behavior when injected into the cerebral ventricles, suggesting that these endogenous peptides may play functional roles in behavioral regulation. 30 references. (Author abstract modified)

003234 Green, A. R. University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford OX2 6HE, England **Repeated exposure of rats to the convulsant agent flurothyl enhances 5-hydroxytryptamine- and dopamine-mediated behavioural responses.** British Journal of Pharmacology (London). 62(3):325-331, 1978.

The behavioral effects of repeated exposure to the convulsant drug flurothyl were examined to elucidate the therapeutic mechanism of electroconsulvise therapy (ECT). Flurothyl treated rats showed enhanced locomotor activity responses to tranylcpromine and L-dopa, methamphetamine, and apomorphine, apparently as a result of increased dopamine receptor sensitivity. The flurothyl treated animals also showed enhanced activity responses to tranylcypromine and l-tryptophan and to 5-methoxy N,N-diemthyltryptamine, suggesting an increase in postsynaptic 5-hydroxytryptamine sensitivity. Results indicate that repeated flurothyl convulsion has the same effect on behavior as repeated ECT. Since both treatments have been used successfully to treat depression, it is suggested that ECT may act by increasing postsynaptic responses to the monoamine neurotransmitters. 23 references. (Author abstract modified)

003235 Greenblatt, E. N.; Lippa, A. S.; Osterberg, A. C. CNS Research Dept., Lederle Laboratories, Pearl River, NY 10965 **The neuropharmacological actions of amoxapine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 233(1):107-135, 1978.

Neuropharmacological studies were undertaken in rats, mice, and squirrel monkeys to determine the extent to which amoxapine displays neuroleptic like, and antianxiety actions as well as antidepressive activity. The data indicate that demethylation of the terminal nitrogen in a dibenzoxazepine series which displays potent central nervous system depressant properties confers antidepressant activity. The antidepressant activity of amoxapine was demonstrated in laboratory animals by the ability of this compound to inhibit tetrabenazine-induced depression and reserpine-induced hypothermia as well as to enhance yohimbine lethality. The fact that punished responding in squirrel monkeys was present after repeated administration may indicate an antianxiety action of this drug. Following acute administration, amoxapine-like chlorpromazine suppressed reinforced responding. 55 references. (Author abstract modified)

003236 Griffiths, Roland R.; Brady, Joseph V.; Snell, Jack D. Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Relationship between anorectic and reinforcing properties of appetite suppressant drugs: implications for assessment of abuse liability.** Biological Psychiatry. 13(2):283-290, 1978.

A comparison between the anorectic and reinforcing properties of eight phenylethylamine anorectics and cocaine was made using 11 laboratory baboons. A quantitative ratio measure was developed and it was found that cocaine has an anorectic reninforcing ratio that is more than ten times greater than the highest phenyiethamine anorectic. The ordering of these compounds based upon this ratio bears a reasonable correspondence to clinical drug evaluation. The measure may provide information for preclinical evaluation of relative abuse potential of anorectic drugs. 21 references. (Author abstract)

003237 Hall, Nicholas R.; Luttge, William G. Department of Pathology, University of Florida College of Medicine, Gainesville, FL 32610 **Effects of the prostaglandin synthesis inhibitor, indomethacin on estrogen- and estrogen plus progesterone-induced sexual receptivity in ovariectomized rats.** Pharmacology Biochemistry and Behavior. 8(5):597-602, 1978.

Indomethacin, a prostaglandin synthesis inhibitor, was administered to ovariectomized rats to determine whether prostaglandin synthesis is necessary for the display of hormone-induced sexual receptivity. Indomethacin failed to inhibit receptivity induced by estrogen or estrogen plus progesterone. Neither intracerebral nor subcutaneous administration of indomethacin diminished the display of steroid-induced reproductive behavior without also causing a depression in open field activity and, in some cases, gastrointestinal problems and even death. Results suggest that prostaglandin synthesis is not a required step in the mechanism by which estrogen and progesterone exert their behavioral effects. The possibility that prostaglandin E2 and luteinizing hormone releasing hormone synthesis or release might contribute to a collateral mechanism for the induction of sexual receptivity is discussed. 36 references. (Author abstract modified)

003238 Handley, George W.; Calhoun, William H. Department of Psychology, Ohio State University, Lima Campus, 4300 Campus Drive, Lima, OH 45804 **The effects of methylphenidate on repeated acquisition of serial discrimination reversals.** Psychopharmacology (Berlin). 57(1):115-117, 1978.

Fourteen male Sprague-Dawley rats were trained to bar-press for sucrose solution in the presence of one or two stimulus conditions. On each daily training session, the stimulus during which bar-pressing was reinforced was reversed. Rats were trained in this serial discrimination reversal procedure until successive acquisitions of the discrimination were stabilized.

Drug treatments consisting of saline or 0.25, 1.0, 2.0.,4.0.,6.0, or 8.0mg/kg methylphenidate were then administered 20 minutes prior to the daily training sessions. Acquisition of the discrimination was enhanced by low doses of methylphenidate and attenuated by the higher two doses. 13 references. (Author abstract)

003239 Handley, Sheila L.; Thomas, Karin V. Pharmacological Laboratories, Department of Pharmacy, University of Aston, Birmingham B4 7ET, England **Influence of catecholamines on dexamphetamine-induced changes in locomotor activity.** Psychopharmacology (Berlin). 58(3):283-288, 1978.

In mice, central noradrenaline (NA) receptor stimulation by intraperitoneal injection of clonidine or intracerebroventricular injection of NA or alpha-methyl-NA caused marked enhancement of the locomotor stimulant effects of dexamphetamine in doses that were without effect when given alone. A minimally stimulating dose of apomorphine reduced the effect of dexamphetamine. Pimozide and phenoxybenzamine each virtually abolished locomotor stimulation after dexamphetamine, while FLA63 (bis-(4-methyl-1-homo-piperazinylthiocarbony1) caused significant reducation. Phenoxybenzamine also abolished the enhancement by clonidine. The intensity of the dexamphetamine effect and the duration of the apomorphine effect were dose related. Clonidine potentiated apomorphine locomotor stimulation; following this drug combination, the nature of the movements more closely resembled those seen after dexamphetamine. Results suggest the involvement of both NA and dopamine in the dexamphetamine response. 37 references. (Author abstract modified)

003240 Harston, Craig Tucker. Tulane University **The effects of D-Ala2-Met5-Enkephalinamide on behavioral activity and cyclic nucleotides in the rat brain. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7807654, HC$15. MF$7.50. 86 p. 1977.

To test whether intracranioventricular endorphins increase activity following an initial decrease, as morphine does, a chronic cannula was stereotaxically implanted into the right lateral ventricle of albino rats. Seventeen to 18 days postsurgery, either 10ul saline, 12.5, 25, 50, or 100ug d-ala2-met5-enkephalinamide (ENK) was injected ICV or 10ug/kg morphine was injected i.p. When behavior was observed after injection, all doses of ENK were found to initially decrease and then increase quadrant crossing, rearing and photocell interruptions. Grooming was decreased by all doses and head movement was decrased by the two highest doses of ENK. Wet dog shakes were observed for all ENK groups shortly after injection. A second group of rats were treated similarly, then sacrificed with microwave radiation. Morphine and ENK were found to have decreased both behavioral activity and cyclic-guanosine monophosphate (cGMP) levels in the midbrain, however, striatal cGMP levels were increased. It is concluded that the changes of activity by ENK were similar to those reported earlier for morphine and the increased activity may have been due to direct effects of ENK; ENK and morphine had a relatively specific effect on cGMP levels because cyclic-adenosine monophosphate levels were unchanged. (Journal abstract modified)

003241 Hayes, R. L.; Price, D. D.; Bennett, G. J.; Wilcox, G. L.; Mayer, D. J. Neurobiology and Anesthesiology Branch, National Institute of Dental Research, National Institutes of Health, Bethesda, MD 20014 **Differential effects of spinal cord lesions on narcotic and non-narcotic suppression of nociceptive reflexes: further evidence for the physiologic multiplicity of pain modulation.** Brain Research (Amsterdam). 155(1):91-101, 1978.

The effects of bilateral lesions of the dorsolateral funiculus (DLF) of the rat spinal cord on the inhibition of a nociceptive reflex produced either by a systemic injection of 4 mg/kg of morphine or by a 20 sec exposure to 1.0mA of transcutaneous electric shock were examined using 90-day old female - Sprague-Dawley rats. Lesions which included only the DLF reduced morphine produced analgsia (MA) by 73% but had no effect on shock produced analgesia (SA) observed in the same rats. Baseline tail flick latencies of this group were not affected by the lesions. Control lesions restricted to the dorsal columns attenuated neither MA nor SA. Lesions which included both the dorsal columns and DLF did no affect SA and produced no greater reduction in MA than t lesions of the DLF alone. he data indicate that supraspinal modulation participating in two different types of analgesic induction involves separate descending spinal pathways and that the maximal expression of analgesia produced by administration of narcotics requires the integrity of a supraspinal neural system projecting in the DLF. 4 references. (Author abstract modified)

003242 Hayes, Ronald L.; Bennett, Gary J.; Newlon, Pauline G.; Mayer, David J. Neurobiology and Anesthesiology Branch, National Institute of Dental Research, National Institutes of Health, Bethesda, MD 20014 **Behavioral and physiological studies of non-narcotic analgesia in the rat elicited by certain environmental stimuli.** Brain Research (Amsterdam). 155(1):69-90, 1978.

The analgesic effects of both noxious and nonnoxious but stressful manipulations in Sprague-Dawley rats were examined. Analgesia was inferred primarily by the observation of reduced responsivity to noxious stimuli as measured by spinally mediated reflexes and more complexly organized behaviors. The results of complete spinal cord transection and the effects of pretreatment with naloxone and chlordiazepoxide were also studied. The efficacy of classical conditioning procedures in attenuating responses to noxious stimuli were evaluated. The results suggest that: 1) the selective modulation of nociceptive input at the level of the spinal cord can be mediated by a supraspinal system or systems physiologically distinct from those involved in analgesia produced by the administration of opiates; 2) nonnarcotic modulation of nociceptive input occurring with the spinal cord can be learned by exposure to classical conditioning procedures; and 3) noxious stimuli are sufficient but not necessary to produce a nonnarcotic analgesia; stress alone, however, is not always sufficient to produce this analgesia. 47 references. (Author abstract modified)

003243 Hendel, Robert C.; Turek, Fred W. Department of Biological Sciences, Northwestern University, Evanston, IL 60201 **Suppression of locomotor activity in sparrows by treatment with melatonin.** Physiology & Behavior. 21(2):275-278, 1978.

The effects of melatonin on locomotor activity were examined in male house sparrows (Passer domesticus). Continuous administration of melatonin via intraperitoneally placed Silastic capsules resulted in a clear reduction in the total amount of perch hopping activity recorded from sparrows maintained on 3/21 or 8/16 light/dark cycles. Removal of the melatonin filled capsules restored the level of locomotor activity to that seen prior to capsule implantation. Evidence suggests that the pineal product melatonin plays a role in both the timing and the amount of activity expressed throughout the activity/rest cycle in birds. 25 references. (Author abstract)

003244 Horowski, Reinhard. Schering AG, Berlin/Bergkamen, Special Research Project Group, Mullerstrasse 170-178, D-1000 Berlin 65, Germany **Differences in the dopaminergic effects of the ergot derivatives bromocriptine, lisuride and d-LSD as compared with apomorphine.** European Journal of Pharmacology (Amsterdam). 51(2):157-166, 1978.

Pretreatment with sulpiride inhibited the hypothermia but not the sterotyped behavior induced by apomorphine or lisuride in normal female NMRI mice. In reserpine pretreated mice, apomorphine, lisuride, d-lysergic acid diethylamide (d-LSD), and bromocriptine restored motor activity, antagonized reserpine induced hypothermia, and (with the exception of bromocriptine) produced stereotyped behavior. Low doses of sulpiride completely abolished the effects of bromocriptine in reserpinized mice, while high doses of sulpiride had little or no effect on the activity of the other dopaminergic agonists in reserpinized mice. Inhibition of tyrosine hydroxylase by alpha-metyle-p-tyrosine completely prevented the effects of bromocriptine, but only slightly affected lisuride and d-LSD activity, and did not alter apomorphine activity. It is suggested that bromocriptine may exert its effects via an inhibitory influence on presynaptic dopamine receptors and that this effect can be counteracted by sulpiride. 28 references. (Author abstract modified)

003245 Hosutt, Jean A.; Rowland, Neil; Stricker, Edward M. Department of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Hypotension and thirst in rats after isoproterenol treatment.** Physiology & Behavior. 21(4):593-598, 1978.

The relationship between blood pressure and water intake in nephrectomized male Sprague-Dawley rats given isoproterenol was examined. When arterial blood pressure was partially elevated by central administration of angiotensin II or carbachol or by intraarterial infusion of epinephrine, drinking behavior was restored in nephrectomized animals and their water intakes approximated the amounts consumed by intact rats given isoproterenol. In general, an inverted U-shaped curve defined the relation between blood pressure and water intake in rats after isoproterenol treatment. Drinking was more probable when mean arterial blood pressures were in the range of 70-85mm Hg, whereas rats were unlikely to drink when blood pressures were much below or above this range. These findings indicate that isoproterenol induced thirst is not dependent on renal dipsogen, and suggest that the hypersecretion of renin that occurs in intact rats is simply permissive of drinking behavior by modulating the hypotensive effects of the drug treatment. 28 references. (Author abstract)

003246 Howard, J. L.; Jones, C. N.; McBennett, S. T. Department of Pharmacology, Wellcome Research Laboratories, Research Triangle Park, NC 27709 **Discriminative stimulus properties of antidepressants.** Psychopharmacology (Berlin). 58(2):6, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the discriminative stimulus properties of bupropion was reported. A two choice discrimination was established in rats rewarded with 45mg food pellets on a fixed ratio 10 schedule of reinforcement for pressing one lever after injection with bupropion (20mg/kg i.p.)and the other lever after saline. Approximately 70% of the subjects reached criterion performance in a mean of 40 training sessions. Discrimination training was not successful after 10mg/kg bupropion, a dose closer to that at which antitetrabenazine effects are seen. In animals trained to discriminate 20mg/kg bupriopion from saline, partial and inconsistent transfer effects were observed to the tricyclic antidepressants (amitriptyline, imipramine, and nortriptyline). In light of previous failures to establish tricyclic antidepressants or monoamine oxidase inhibitor antidepressants as discriminative stimuli, these findings suggest that there is no distinctive antidepressant stimulus cue common to drugs with clinical antidepressant effects. 2 references. (Author abstract modified)

003247 Huston, Joseph P.; Staubli, Ursula. Institute of Psychology, Laboratory of Comparative and Physiological Psychology, University of Dusseldorf, Dusseldorf, Germany **Retrograde amnesia produced by post-trial injection of substance P into substantia nigra.** Brain Research (Amsterdam). 159(2):468-472, 1978.

The effects of posttrial intranigral injection of substance-P on learning of a passive avoidance task were investigated in male Sprague-Dawley rats. Administration of 500ng substance-P 30 seconds after footshock led to retrograde amnesia for passive avoidance learning, presumably as a result of activation of the dopaminergic (DA) nigroneostriatal bundle and the release to excessive DA in the caudate neucleus, Administration of 30 second delayed posttrial substance-P in a dose of 50ng or a 3 hour delayed substance-P in a dose of 500ng failed to induce amnesia. 24 references.

003248 Ito, Hirosumi. Department of Physiology, College of Medicine, University of Utah, 410 Chipeta Way, Room 156, Research Park, Salt Lake City, UT 84108 **Preference behavior and taste nerve responses in D-penicillamine treated rats.** Physiology & Behavior. 21(4):573-579, 1978

Preferences for sodium chloride (NaCl), sucrose, hydrochloride (HCl), and quinine were examined in male Wistar rats fed a diet containing D-penicillamine (D-pen). Preferences for NaCl and sucrose were reduced by administration of D-pen and returned to normal upon cessation of D-pen administration. Change in preferences for NaCl and sucrose depended on the amount and duration of D-pen administration. Preferences for HCl and quinine were unaffected by D-pen. No significant difference in the threshold and magnitude of the chorda tympani nerve responses to the taste stimuli was found between D-pen treated and normal rats. Concentrations of electrolytes in serum and saliva were scarcely changed by D-pen administration, but the amount of serum copper was markedly reduced. The effect of D-pen on sensitivity of taste receptors and the role of copper ions in regulating fluid intake are discussed. 16 references. (Author abstract)

003249 Jarbe, Torbjorn U. C.; Rollenhagen, Carl. University of Uppsala, Department of Psychology, P.O. Box 227, S-75104 Uppsala, Sweden **Morphine as a discriminative cue in gerbils: drug generalization and antagonism.** Psychopharmacology (Berlin). 58(3):271-275, 1978.

Gerbils were trained in an electrified T-maze to discriminate between one of three training doses of morphine (8, 16, or 32mg/kg) and the nondrug condition. The rate of acquisition of the morphine discriminations was dose dependent, and dose generalization tests showed that higher training doese of morphine produced correspondingly higher median effective dose (ED50) values in producing 50% morphine appropriate responding. Antagonism of the discriminable effects of morphine by naltrexone (0.025-0.40mg/kg) was also dose related, with higher training doese of morphine resulting in correspondingly higher ED50 values for blockade by naltrexone. A stereoisomeric requirement for morphine discrimination was evident, since levorphanol, but not the analgesically inactive dextrophan, yielded morphine appropriate responses when tested by substitution. 28 references. (Author abstract modified)

003250 Jarbe, Torbjorn U. C. University of Uppsala, Department of Psychology, P.O. Box 227, S-75104 Uppsala 1, Sweden **Cocaine as a discriminative cue in rats: interactions with neuroleptics and other drugs.** Psychopharmacology (Berlin). 59(2):183-187, 1978.

Male Sprague-Dawley rats were trained to discriminate between the effects of 4mg/kg of cocaine hydrochloride and saline in a T-shaped maze. In subsequent test trials, the median effective dose of cocaine was 1.6mg/kg; the duration of the discriminable effects of cocaine in producing 50% cocaine appropriate

responding was 57.9minutes postinjection. Pretreatment with neuroleptics (pimozide, haloperidol, and chlorpromazine), but not with propranolol, phenoxybenzamine, alpha-methyl-para-tyrosine, or physostigmine, attenuated the cocaine discrimination. Results are discussed with reference to previous findings in amphetamine discriminations. 30 references. (Author abstract modified)

003251 Jordan, L. M.; Kenshalo, D. R., Jr.; Martin, R. F.; Haber, L. H.; Willis, W. D. Marine Biomedical Institute, University of Texas Medical Branch, Galveston, TX 77550 **Depression of primate spinothalamic tract neurons by iontophoretic application of 5-hydroxytryptamine.** Pain (Amsterdam). 5(2):135-142, 1978.

The effects of iontophoretic applications of 5-hydroxytryptamine (5-HT) were tested upon primate spinothalamic tract neurons recorded extracellularly in the spinal cord of anesthetized monkeys. The activity of most high threshold and wide dynamic range spinothalamic tract cells was depressed. 5-HT also reduced the responses of the cells to glutamate pulses which by themselves had a powerful excitatory action. It is concluded that 5-HT has a depressant action upon the postsynaptic membranes of spinothalamic tract cells, although the action has a slow time course. Results support the hypothesis that serotonergic pathways descending from the brainstem produce a postsynaptic inhibition of spinothalamic tract neurons. 35 references. (Author abstract)

003252 Jouhaneau, Jacques; Le Magnen, Jacques. Laboratoire de Neurophysiologie sensorielle et comportementale, College de France 11, Place Marcelin Berthelot, F-75231 Paris-Cedex, France **Food related intravenous insulin self-administration in normal and diabetic rats.** Physiology & Behavior. 20(6):739-747, 1978.

Rats learned to press a lever for administration of insulin or saline through a chronic cardiac catheter. The average daily amount of self-injected insulin was five times that of saline. Ninety percent of the daily insulin intake (compared to 50% for saline) was injected at mealtime or shortly afterwards, and the amount of periprandial self-injected insulin correlated positively with the size of the meal. Fasted rats showed an immediate drop in the amount of self-administered insulin. Upon discontinuation of insulin delivery, rats continued to press the inoperant lever in the same previously established meal related pattern. Daily food and water intake and body weight gain did not differ in insulin treated rats and controls. In diabetic rats previously trained on insulin self-injection, a transitory increase in daily insulin intake was observed which later stabilized at a level lower than the prediabetic one. Results are discussed in relation to the reinforcing property of insulin and to neuroendocrine mechanisms of food intake. 8 references. (Author abstract modified)

003253 Kafi, Sarah; Gaillard, Jean-Michel. Clinique Psychiatrique de l'Universite de Geneve, Bel-Air, CH-1225 Chene-Bourg, Switzerland **Biphasic effect of chlorpromazine on rat paradoxical sleep: a study of dose-related mechanisms.** European Journal of Pharmacology (Amsterdam). 49(3):251-257, 1978.

The effect of chlorpromazine (CPZ), alone or in combination with catecholamine (CA) synthesis inhibitors, on paradoxical sleep (PS) was investigated in male Wistar rats. The dose response curve for CPZ was biphasic, with enhancement of PS after low doses and depression of PS after higher doses. After inhibition of CA synthesis, however, low doses of CPZ markedly decreased PS; this decrease was greater after tyrosine hydroxylase inhibition by alpha-methyl-p-tyrosine than after dopamine-beta-hydroxylase inhibition by FLA63. Results suggest that low doses of CPZ produce increased activity in brain CA synapses and that both dopamine and norepinephrine participate in the control of PS in the rat. 35 references. (Author abstract modified)

003254 Kallman, M. J.; Rosecrans, J. A.; Glennon, R. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Discriminative stimulus properties of nicotine: organic molecular mechanisms and neurochemical events.** Psychopharmacology (Berlin). 58(2):7, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the generalization of the nicotine discriminative cue to other nicotine and pyridine derivatives was reported. Rats were trained to discriminate 200ug, kg subcutaneous nicotine from saline in a two bar discrimination task, reinforced with sweetened milk on a variable interval 15 second schedule of delivery. Several nicotine-like compounds were tested across a wide dose range for generalization to the nicotine trained cue. Two of the compounds tested, 3-pyridyl-methylpyrollodine and nornicotine, had significant generalization to the nicotine-like activity via central nicotinic receptors. Nicotine-like activity was dependent on an intact pyrollidine ring and decreased when the length of the N-site chain was increased. (Author abstract modified)

003255 Katz, R. J.; Carroll, B. J. Mental Health Research Institute, Department of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Inhibition of phenylethanolamine-N-methyltransferase and brain-stimulated reward.** Psychopharmacology (Berlin). 57(1):39-42, 1978.

The effects of three centrally active inhibitors of phenylethanolamine-N-methyl transferase, the terminal enzyme for epinephrine biosynthesis in the brain, on self-stimulation behavior in the male Sprague-Dawley rat were investigated. All three compounds produced dose related decreases in rates of responding for rewarding brain stimulation; decreases occurred at dosages that did not produce measurable neurologic impairment. Findings suggest that the catecholamine theory of reward may be extended to include central epinephrine containing neurons, in addition to those containing dopamine and norepinephrine, in the maintenance of reward mediated behaviors. 28 references. (Author abstract modified)

003256 Kay, David C.; Martin, William R. National Institute on Drug Abuse, Division of Reserach, Addiction Research Center, Lexington, KY 40583 **LSD and tryptamine effects on sleep/wakefulness and electrocorticogram patterns in intact cats.** Psychopharmacology (Berlin). 58(3):223-228, 1978.

The effects of intravenous infusions of lysergic acid diethylamide (LSD: 3.75, 7.5, or 15mcg/kg over 5 minutes) and tryptamine (0.04, 0.08, or 0.12mg/kg/minute) were compared to saline in intact cats through observation of five sleep/waking patterns. LSD increased wakefulness and drowsiness and decreased spindle sleep and rapid eye movement (REM) sleep during the first 75 minutes (period 1). The increase in active wakefulness and decrease in REM sleep persisted during period 2, with an increase in spindle sleep thereafter. LSD increased delta index and electrocorticogram (ECoG) amplitude, with a decrease in ECoG frequency; these effects peaked in period 2. Tryptamine increased wakefulness and drowsiness during period 1, with decreases in spindle sleep and REM sleep. The increase in quiet wakefulness and decrease in REM sleep persisted during period 2, but no significant tryptamine effect was seen in sleep/waking patterns after infusion ceased. ECoG frequency increased during tryptamine infusion (periods 1 and 2), while amplitude increased during periods 2 and 3. Thus, LSD and tryptamine both increased wakefulness, decreased spindle sleep, and decreased REM sleep. 24 references. (Author abstract modified)

003257 Kehne, John H.; Sorenson, Charles A. Psychology Department, Amherst College, Amherst, MA 01002 **The effects of pimozide and phenoxybenzamine pretreatments on amphetamine and apomorphine potentiation of the acoustic startle response in rats.** Psychopharmacology (Berlin). 58(2):137-144, 1978.

The role of neurons containing norepinephrine (NE) and dopamine (DA) in modulating the amplitude of the acoustic startle response (ASR) in rats was investigated. Treatment with pimozide (2.5mg/kg) and phenoxybenzamine (10mg/kg) resulted in a significant reduction in startle amplitude. The startle potentiating effects of d-amphetamine, l-amphetamine, and apomorphine were totally blocked by pretreatment with pimozide. Phenoxybenzamine pretreatment blocked the startle potentiating effects of l-amphetamine and apomorphine, but not of d-amphetamine. Results indicate that neurons containing NE and DA both tonically facilitate the ASR. The startle potentiating effects of amphetamine and apomorphine appear to be due at least in part to increased activity at central DA receptors. Noradrenergic neurons may also be involved in the potentiation of the ASR by these agents, possibly through the interaction of dopaminergic and noradrenergic neural systems. 23 references. (Author abstract modified)

003258 Kishi, Reiko; Hashimoto, Keigo; Shimizu, Shinichiro; Kobayashi, Miya. Department of Public Health, Sapporo Medical College, Minami-1, Nishi-17, Chuo-Ku, Sapporo 060, Japan **Behavorial changes and mercury concentrations in tissues of rats exposed to mercury vapor.** Toxicology and Applied Pharmacology. 46(3):555-556, 1978.

Critical brain mercury concentrations associated with specific behavioral changes during exposure to mercury (Hg) vapor were determined in male rats. Animals exposed to Hg (3mg/m3) for 3 hours, 5 days per week, for 15 to 42 weeks showed a decline in conditioned avoidance response. The latency of escape response also increased in pole climb shock escape. The time to the onset of the effects varied form 12 to 39 weeks among 14 rats exposed to Hg. All rats recovered to preexposure baseline within 12 weeks after the termination of exposure. A significantly poor behavioral performance was seen in rats with brain Hg concentrations of approximately 20microg/g brain tissue. Results suggest that the critical concentration of inorganic mercury in the brain associated with behavioral changes in the rat ranges from 10-20 parts per million. In spite of the high concentrations of Hg, the nervous tissues of rats with Hg vapor intoxication in this experiment were normal. 15 references. (Author abstract)

003259 Kodama, J.; Fukushima, M.; Sakata, T. First Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, 812 Japan **Diminished taste reactivity to saccharin following chronic administration of theophylline in rats.** Physiology & Behavior. 21(4):647-652, 1978.

The effect of theophylline on acceptance or rejection responses to saccharin at both facilitatory and inhibitory concentrations was investigated in adult male Wistar King A-strain rats. Under a successive increase in the concentration of saccharin adulteration, a dual effect of facilitation and inhibition of food intake was observed. At low concentrations (0.25 to 1.5%), saccharin adulterated diets were more acceptable than the normal diet, with peak acceptance at 1.0% concentration. Food intake was suppressed at a high concentration (3.0%). On exposure to either 1.0or 3.0% saccharin diet, this facilitatory or inhibitory effect disappeared with chronic administration of theophylline. This diminution of acceptance or rejection response to saccharin suggests an impairment of taste discrimination induced by theophylline. 21 references. (Author abstract)

003260 Kokkinidis, Larry; Anisman, Hymie. Department of Psychology, Carleton University, Ottawa, Ontario, K1S 5B6, Canada **Abatement of stimulus perservation following repeated d-amphetamine treatment: absence of behaviorally augmented tolerance.** Pharmacology Biochemistry and Behavior. 8(5):557-563, 1978.

The effect of chronic d-amphetamine treatment on stimulus perservation was examined in mice. Acute administration of amphetamine resulted in perservation between two compartments when animals were placed in a free running Y-maze exploratory situation. This perseverative behavior was attenuated by making the arms of the maze distinctively different or by repeated amphetamine treatment. Drug-induced locomotor behavior and stereotypy were not affected by chronic drug administration. The course of the tolerance effect was not altered by pairing the repeated drug experience with Y-maze exposure. It is concluded that although stimulus factors are involved in the perseverative response, conditioning factors are not of primary relevance in determining the tolerance. The mechanisms which subserve stimulus perseveration appear to be different from those which mediate locomotor activity and stereotypy. 34 references. (Author abstract modified)

003261 Kostas, Jeanne; McFarland, D. J.; Drew, W. G. Laboratories of Behavioral Neurophysiology, Dept. of Psychiatry, University of Kentucky Medical Center, Lexington, KY 40506 **Lead-induced behavioral disorders in the rat: effects of amphetamine.** Pharmacology (Basel). 16(4):226-236, 1978.

The effects of d-amphetamine on several measures of activity and spontaneous alternation were evaluated in Long-Evans hooded rats chronically exposed to a low level of lead acetate via maternal milk during the neonatal period to examine complexities in the relationship between the effects of a drug and the measurement of activity. Alterations in the amphetamine responses of lead treated rats were observed with some measures of activity and exploration but not with others. Paradoxical responses were observed with postural rearing and spontaneous alternation, and no drug response was seen in lead treated animals with respect to center field activity in contrast to a large increase seen in controls. Normally, amphetamine reduces grooming behavior, but since this reduction was greater in lead reared than in control rats, the data suggest that for this measure the lead reared rat may possess an increased sensitivity to amphetamines. The results are discussed in terms of the behavioral parallels found between lead poisoning and childhood hyperactivity as well as the potential of this model as an animal analog of minimal brain dysfunction hyperactivity. 48 references. (Author abstract)

003262 Koupilova, M.; Fusek, J.; Hrdina, V. Purkyne Medical Research Institute, 50260 Hradec Kralove, Czechoslovakia **Tacrine and its derivatives antagonize cholinergic psychotomimtics: behavioural study in rats.** Activitas Nervosa Superior (Praha). 20(1):76-77, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, a behavioral study of the action of tacrine and its derivative in antagonizing cholinergic psychotomimetics is reported. Testing of therapeutic efficacy after intoxication by a psychotomimetic indicates that 9-amino-7-methoxy-1,2,3,4-tetrahydroacridine (TAO3) has the best effect of a number of tacrine derivatives. Both acquisition of conditioned avoidance reactions and performance of previously learned avoidance behavior were influenced.

003263 Kovacs, Gabor L.; Vecsei, Laszlo; Telegdy, Gyula. Department of Pathophysiology, University Medical School

Szeged, Hungary **Opposite action of oxytocin to vasopressin in passive avoidance behavior in rats.** Physiology & Behavior. 20(6):801-802, 1978.

The effects of oxytocin and lysine-8-vasopressin on step down passive avoidance behavior was studied in rats. Step down latency was considerably shortened after treatment with oxytocin and lengthened by vasopressin. Findings suggest opposite actions of oxytocin and vasopressin on step down latency, probably as a result of opposite effects on memory consolidation. 18 references. (Author abstract modified)

003264 Kraly, F. Scott; Carty, William J.; Resnick, Steven; Smith, Gerard P. Dept. of Psychology, Colgate University, Hamilton, NY 13346 **Effect of cholecystokinin on meal size and intermeal interval in the sham-feeding rat.** Journal of Comparative and Physiological Psychology. 92(4):697-707, 1978.

The effects of the putative satiety signal cholecystokinin (CCK) on feeding behaviors in the rat were investigated. Meal size was larger, latency to rest after a meal was longer, and intermeal interval was shorter during sham feeding than during normal feeding. CCK decreased meal size and latency to rest, and increased intermeal interval during sham feeding. Results demonstrate that the preabsorptive food contingent stimuli of sham feeding plus exogenous CCK are sufficient for normal short-term satiety under certain conditions, and they provide evidence consistent with the hypothesis that cholecystokinin produces satiety in rats. 18 references. (Author abstract modified)

003265 Krejci, I.; Kupkova, B. Research Institute for Pharmacy and Biochemistry VUFB, Kourimska 17, 13060 Prague, Czechoslovakia **Sleep-inducing effect of a vasopressin analog, deamino-6-carba-ornithine-8-vasopressin (DCOV) in rats.** Activitas Nervosa Superior (Praha). 29(1):60-61, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the sleep inducing effect of a vasopressin analog, deamino-6-carba-ornithine-8-vasopressin (DCOV), in rats is described. DCOV given to male Wistar rats reduced exploratory activity and proportionally prolonged immobility. With higher doses, activity was restricted to a few minutes at the beginning of the session. It is noted that after that period, most rats lay down and close their eyes, manifesting no signs of ataxia or catalepsy. These unexpected findings are discussed in terms of the chemical structure of the vasopressin analog. 2 references.

003266 Krimmer, E. C.; Barry, H., III; Coltrin, D. Department of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15261 **Antagonism of pentobarbital discriminative stimulus by bemegride in immobilized rats.** Psychopharmacology (Berlin). 58(2):7, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the antagonism of the pentobarbital discriminative stimulus by bemegride in immoblized rats was reported. The drug increased the number of pentobarbital correct head turns and the total number of head turns in either direction in a water reinforced two choice discrimination task. Most bemegride doses (1.25-25mg/kg, i.p.,simultaneously with pentobarbital) partially antagonized the effect of most pentobarbital doses (10-25mg/kg) on both measures of performance. With high pentobarbital doses, however, low bemegride doses increased both measures of performance, indicating antagonism of the behaviorally depressant or toxic effects but not of the discriminative effects of pentobarbital. It is concluded that, in body restraint conditions, low doses of bemegride selectively antagonize the behaviorally depressant effect of toxic pentobarbital doses, without attenuating the discriminative pentobarbital stimulus. (Author abstract modified)

003267 Ksir, Charles; McKearney, James W. Department of Psychology, University of Wyoming, P. O. Box 3415, University Station, Laramie, WY 82071 **Pentobarbital, promazine, d-amphetamine, and scopolamine effects on behavior under multiple and primed schedules of reinforcement.** Psychopharmacology (Berlin). 59(2):205-207, 1978.

The effects of pentobarbital, promazine, d-amphetamine, and scopolamine on the behavior of adult male White Carneaux pigeons under multiple and primed schedules of reinforcement were examined. Pigeons responded under compound fixed interval (FI) fixed ratio (FR) schedules of food presentation. Distinctive discriminative stimuli were either continuously present during each component schedule (multiple FI FR) or were present only for a brief period at the beginning of each component (primed FI FR). Similar rates and patterns of responding were maintained under the multiple and primed schedules. Pentobarbital, scopolamine, and d-amphetamine decreased FR responding, while promazine had little effect. Promazine and d-amphetamine increased FR responding at certain doses, while scopolamine decreased responding and pentobarbital had little effect. No systematic differences were found in the effects of drugs under the multiple and primed schedules, in spite of the differences in discriminative stimuli under the conditions. 5 references. (Author abstract modified)

003268 Kubie, John L.; Vagvolgyi, Alice; Halpern, Mimi. Dept. of Physiology, University of Pennsylvania Medical School, Philadelphia, PA **Roles of the vomeronasal and olfactory systems in courtship behavior of male garter snakes.** Journal of Comparative and Physiological Psychology. 92(4):627-641, 1978.

The roles of the vomeronasal and olfactory systems in courtship behavior of male garter snakes were investigated via bilateral olfactory nerve cuts, vomeronasal nerve cuts, and control surgeries. Male garter snakes (Thamnophis radix) with testosterone propionate pellets implanted subcutaneously were tested for courtship displays with estradiol benzoate treated females. Data indicate that male garter snakes without functional olfactory systems do court and mate normally, but that male garter snakes without functional vomeronasal systems exhibit no courtship responses. 38 references. (Author abstract modified)

003269 Kuribara, Hisashi. Behavior Research Institute, School of Medicine, Gunma University, 3-39-22 Showa-machi, Maebashi 371, Japan **Psychotropic drugs and Sidman avoidance in rats: IRT distribution changes.** Pharmacology Biochemistry and Behavior. 8(5):537-542, 1978.

The effects of d-amphetamine, caffeine, chlorpromazine, diazepam, and pentobarbital on Sidman avoidance responsing were examined in rats. Amphetamine and caffeine increased the total number of responses and the number of short interresponse times (IRTs) and decreased the number of longer IRTs. Chlorpromazine, diazepam, and pentobarbital increased the number of shocks delivered. No marked change in total number of responses was observed after chlorpromazine, but response bursts and escape responses increased and long IRTs increased after diazepam or pentobarbital, and the total number of responses was decreased by both drugs. Results indicate that, when using the Sidman avoidance procedure for psychotropic drug assessment, changes in the IRT distribution give a more precise profile of the drug than is afforded by the total number of responses and shocks delivered. 23 references. (Author abstract modified)

003270 Lal, H.; Miksic, S.; McCarten, M. Department of Pharmacology and Toxicology, University of Rhode Island, Kings-

ton, RI 02881 **A comparison of discriminative stimuli produced by naloxone, cyclazocine and morphine in the rat.** Psychopharmacology (Berlin). 58(2):8, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a comparative study of the discriminative stimuli produced by naloxone, cyclazocine, and morphine was reported. Male rats were trained to press a lever on one side of a food cup after a drug injection and on the other side after a saline injection in a fixed-ratio 10 schedule of food reinforcement. Animals readily acquired morphine (10mg/kg) - saline and cyclazocine (1.25mg/kg) - saline discriminations. Naloxone (10mg/kg) - saline discrimination could not be learned until the subjects were given morphine experience (40mg/kg morphine, 8-18 hours before each training session). Each drug generalized to its own training dose according to linear log dose response curves. Morphine generalized to cyclazocine but not to naloxone. Naloxone did not generalize to morphine or cyclazocine and antagonized the discriminative stimuli of both. Cyclazocine and pentazocine generalized to morphine in inverted U-shaped dose response curves. It was concluded that drug discrimination may be a useful technique in studying mechanisms of central subjective effects of narcotic antagonists. (Author abstract modified)

003271 Lassen, J. Buus. Department of Pharmacology, A/S Ferrosan, Sydmarken 5, DK-2860 Soeborg, Denmark **Influence of the new 5-HT-uptake inhibitor paroxetine on hypermotility in rats produced by p-chloroamphetamine (PCA) and 4,alpha-dimethyl-m-tyramine (H 77/77).** Psychopharmacology (Berlin). 57(2):151-153, 1978.

The effects of paroxetine on two forms of hypermotility produced by the amphetamine derivatives p-chloroamphetamine (PCA) and 4,alpha-dimethyl-m-tyramine (H 77/77) were studied in female Wistar rats Subcutaneous injections of paroxetine inhibited the effect of PCA but did not influence that of H 77/77. PCA hypermotility was also inhibited by oral administration of paroxetine, imipramine, or chlorimipramine. Paroxetine 0.5to 2mg/kg was active at intervals of 1 to 4 hours; 4mg/kg paroxetine was active at 18 hours. Imipramine and chlorimipramine, 25 to 30mg/kg, inhibited PCA hypermotility at treatment intervals of 1 to 2 hours, but 80 to 100mg/kg or more was required to inhibit PCA at intervals of 4 and 18 hours. Findings indicate that paroxetine selectively inhibits uptake of 5-hydroxytryptamine (5-HT) and produces more potent and longer lasting 5-HT uptake inhibition than imipramine and chlorimipramine. 23 references. (Author abstract modified)

003272 Leibowitz, Sarah Fryer. Rockefeller University, New York, NY 10021 **Adrenergic stimulation of the paraventricular nucleus and its effects on ingestive behavior as a function of drug dose and time of injection in the light-dark cycle.** Brain Research Bulletin. 3(4):357-363, 1978.

The effects of norepinephrine (NE) on the paraventricular nucleus (PVN) (the most responsive site in the brain for eliciting feeding and preprandial drinking responses) as a function of dose and time of injection in the light/dark cycle was investigated in two experiments with 44 male albino Sprague-Dawley rats. The lowest effective doses for producing ingestive responses with exogenous NE in the PVN were found to be between 5.6ng and 16.9ng for preprandial drinking and between 1.0ng and 4.2ng for feeding. Tests with NE injection into the PVN at different times of the light/dark cycle indicated that an increase in feeding effect could occur in the dark as well as in the light and at varying levels of food intake baseline and with solid and liquid food. It is concluded that site of injection in the brain is a crucial factor in determining the nature of NE's effects on feeding behavior. 29 references. (Author abstract modified)

003273 Leite, Jose Roberto. Departamento de Psicobiologia, Escola Paulista de Medicina, Rua Botucatu, 862, 04023 Sao Paulo, Brazil **Effects of chronic ingestion and withdrawal of sodium barbitone on learning in rats.** Psychopharmacology (Berlin). 57(2):205-209, 1978.

The effects of chronic barbitone administration and its withdrawal on the acquisition of appetitive and aversive reinforced behaviors were examined in Wistar rats. The animals were submitted to three different manipulations: 1) chronic ingestion of barbitone in drinking water; 2) chronic administration of barbitone and subsequent withdrawal of the drug, and 3) drinking water only. Both drug groups showed deficient acquisition in shuttlebox avoidance and passive avoidance response, as compared to the water only animals. However, no impairment was observed in passive avoidance response when the withdrawal period was extended from 2 to 15 days, and no impairment was seen when animals were tested in a T-maze or in another appetitive task. 10 references. (Author abstract modified)

003274 Lemmer, B.; Berger T. Zentrum der Pharmakologie, Johann Wolfgang Goethe-Universitat, Theodor-Stern-Kai 7, D-6000 Frankfurt am Main 70, Germany **Diurnal variations in the motor activity of the rat: effects of inhibitors of the catecholamine synthesis.** Naunyn-Schmiedeberg's Archives of Pharmacology. 303(3):251-256,1978.

The effects of the inhibitor of the tyrosine-hydroxylase H 44/68 and the inhibitor of the dopamine-beta-hydroxylase FLA 63 on the on the diurnal variations of the motor activity was studied in male Wistar rats kept under standardized conditions of light and darkness. The motor activity was continuously registered in groups of five rats using a two channel Animex motimeter. During light FLA 63 greatly increased motor acitivity on acute application and during darkness the physiological elevation in motor activity was further but slightly increased. H 44/68 also increased motor activity during darkness. The results indicate that though dopamine and noradrenaline are involved in the regulation of behavioral components, one or the other catecholamine may play a predominant role at different times of the day. It is concluded that studying the effects of drugs separately during light and during darkness might prove to be a worthwhile endeavor. 25 references. (Journal abstract modified)

003275 Lesher, Gary A.; Spratto, George R. Department of Pharmacology and Toxicology, School of Pharmacy, University of Maryland, Baltimore, MD 21201 **Potentiation of hexobarbital and amphetamine effects in male and female rats physically dependent on morphine.** Psychopharmacology (Berlin). 57(2):175-183, 1978.

The pharmacologic effect of amphetamine and hexobarbital in the morphine dependent male and female rat was examined as well as the possible mechanisms by which changes in the pharmacologic effect are manifested. Morphine dependence following subcutaneous implantation of 207mg morphine in pellet form increased hexobarbital sleeping time in male and female rats. Only male morphine dependent rats manifested a decrease in in-vitro hepatic metabolism of hexobarbital as well as a significantly faster rate of decline of hexobarbital from the brain. In-vivo uptake of hexobarbital into the brain revealed no difference between male and female and morphine dependent and sham implanted animals. In male rats, morphine dependence also increased amphetamine stimulated locomotor activity, increased brain levels of amphetamine, and decreased in-vitro metabolism of aniline. Morphine dependent female rats showed increases in brain levels of amphetamine, but no other changes were ob-

served. The in-vivo decline of amphetamine from the brain of male and female morphine dependent rats was not significantly different from that of controls. 36 references. (Author abstract modified)

003276 Liebman, Jeffrey; Neale, Robert; Moen, Nancy J. Research Department, Pharmaceuticals Division, Ciba-Geigy Corporation, Summit, NJ 07901 **Differential behavioral effects of sulpiride in the rat and squirrel monkey.** European Journal of Pharmacology (Amsterdam). 50(4):377-383, 1978.

The effects of sulpiride on Sidman avoidance responding were investigated in rats and squirrel monkeys. At 100mg/kg, intraperitonealy or orally, sulpiride failed to impair Sidman avoidance responding in rats. At 30mg/kg orally, however, the drug strongly impaired Sidman avoidance responding in the squirrel monkey. This effect was reversed by benztropine, indicating that dopamine receptor blockade was most likely responsible for the impairment in responding. The gross behavioral effects of sulpiride in the squirrel monkey resembled those of haloperidol, and dyskinetic postures induced by haloperidol could be mimicked by sulpiride in some cases. It is concluded that behavioral effects of sulpiride in the rat may not be representative of its actions in primates or humans. 17 references. (Author abstract modified)

003277 Lloyd, Mary Anne; Appel, James B.; McGowan, William T., III. Alternatives, 1516 Pine Avenue West, Montreal, Quebec, Canada **Effects of morphine and chlorpromazine on the detection of shock.** Psychopharmacology (Berlin). 58(3):241-246, 1978.

The extent to which the perceptual effects of morphine and chlorpromazine (CPZ) can be attributed to drug induced changes in ability to detect shock stimuli was investigated in male Sprague-Dawley rats, using a discrete trial, two choice, yes/no procedure. Both morphine (4.0, 5.0, and 6.0mg/kg) and CPZ (0.25, 0.50 and 1.0mg/kg) significantly reduced accuracy and increased the times to initiate trials and to make choice responses. The effects of morphine appeared to be somewhat greater than those of CPZ, particularly at the lowest shock intensity (0.05mA). When compared to appropriate saline control days, morphine, but not CPZ, significantly reduced accuracy of discrimination on trials when shocks were presented; CPZ, but not morphine, reduced accuracy on no shock trials. The effects of morphine, but not CPZ, on accuracy decreased as shock intensity increased. The effects of shock intensity were generally inversely related to the effects of morphine and directly related to the effects of CPZ. 16 references. (Author abstract modified)

003278 Lucot, James Bernard. University of North Carolina at Chapel Hill **The behavioral effects of d-amphetamine and chlorpromazine in rats; combinations with acute and chronic administration of morphine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 787148, HC$15. MF$7.50. 144 p. 1977.

The behavioral effects of d-amphetamine and chlorpromazine were determined in rats responding under either a fixed-interval 5 min (FI-5) or a multiple fixed-interval 2.5min fixed-ratio 30 (mult FI-2.5FR-30) responses schedule for food presentation. The behavioral effects of d-amphetamine and chlorpromazine were then redetermined in combination with acute doses of morphine, when drinking a 0.5mg/ml morphine solution, when undergoing withdrawal from the morphine solution, and after detoxification from the morphine solution. The FI-5 schedule produced low rates of responding, the FI-2.5component of the multiple schedule produced medium rates of responding, and the FR-30 component produced high rates of responding. Under all baseline rates of responding morphine, chlorpromazine, and d-amphetamine produced dose related decreases in responding. The combination of d-amphetamine with acute doses of morphine produced effects which were greater than, and the combination of chlorpromazine and acute doses of morphine produced effects which were equal to, the sum of the effects of each drug alone. However, it is reported that no change in the behavioral effects of either d-amphetamine or chlorpromazine was seen during morphine drinking, during morphine withdrawal, or after detoxification from morphine. (Journal abstract modified)

003279 Mackenzie, R. G.; Hoebel, B. G.; Norelli, C.; Trulson, M. E. Program in Neuroscience, Department of Psychology, Princeton University, Princeton, NJ 08540 **Increased tilt-cage activity after serotonin depletion by 5,7-dihydroxytryptamine.** Neuropharmacology (Oxford). 17(11):957-963, 1978.

Administration of 5,7-dihydroxytryptamine (5,7-DHT, 8mcg) into the medial forebrain bundle of female Sprague-Dawley rats produced a 78% decrease in forebrain 5-hydroxytryptamine (5-HT) and a twofold increase in 24 hour tiltcage activity. Intraventricular administration of 5,7-DHT (200mcg) resulted in a fourfold increase in 24 hour activity and 5-HT depletions of 83% in the forebrain the, 58% in the brainstem, and 71% in spinal cord. The diurnal index of activity was identical for 5,7-DHT and control groups, suggesting preservation of the normal light/dark activity rhythm. Unlike rats with median raphe lesions, 5,7-DHT treated rats were hypoactive when tested in the open field. Administration of p-chlorophenylalanine (p-CPA) produced a dose dependent increase in tiltcage activity in normal rats, but had relatively little effect on activity in 5,7-DHT treated rats. Although different methods of 5-HT depletion can result in different effects on various behavioral measures, tiltcage hyperactivity was produced by electrolytic raphe lesions, p-CPA, or 5,7-DHT. These results suggest that this effect is not the result of nonspecific damage, but of subnormal 5-HT synaptic activity in the CNS. 15 references. (Author abstract modified)

003280 Maickel, Roger P.; Lambert, Carol S.; Braude, Monique C.; Zabik, Joseph E. School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN 47907 **Behavioral effects of psychotherapeutic agents in rats chronically dosed with alpha-acetylmethadol.** Communications in Psychopharmacology. 2(1):45-50, 1978.

Rats chronically dosed with alpha-l-acetylmethadol (LAAM) prior to acute dosage of various antidepressants, antipsychotics, or anxiolytic agents were then tested in spontaneous motor activity, open field, or rotorod situations in order to determine possible behavioral changes. The only evidence for drug interaction in chronic LAAM rats was seen in a modest decrement of activity and impairment of rotorod performance by imipramine, and in paradoxical increase in open field and actophotmeter activity induced by chlordiazepoxide. 10 references. (Author abstract)

003281 Maj, Jerzy; Sowinska, Helena; Baran, Leokadia; Gancarczyk, Lidia; Rawlow, Andrzej. Institute of Pharmacology, Polish Academy of Sciences, 12 Smetna Street, 31-343 Krakow, Poland **The central antiserotonergic action of mianserin.** Psychopharmacology (Berlin). 59(1):79-84, 1978.

The central antiserotonergic action of mianserin (MS) was tested in mice, rats, and rabbits. Both MS and cyproheptadine inhibited the head twitch response to 5-hydroxytryptophan in mice and rats without affecting the pinna reflex. MS did not change the flexor reflex of the hindlimb of the spinal rat; it antagonized stimulation induced by fenfluramine, lysergic acid diethylamide, and quipazine but not by clonidine. Hyperthermia produced in rabbits by serotonergic stimulants was also antago-

nized by pretreatment with MS. Unlike cyproheptadine, MS was not active in the oxotremorine test. Results indicate that at low doses, MS acts as a central serotonergic receptor blocker. 38 references. (Author abstract modified)

003282 Malick, Jeffrey B. Biomedical Research Department, ICI Americas Inc., Wilmington, DE 19897 **Inhibition of fighting in isolated mice following repeated administration of lithium chloride.** Pharmacology Biochemistry and Behavior. 8(5):579-581, 1978.

The effects of acute (single dose) and subacute (multiple dose) administration of lithium on isolation-induced aggression were examined in mice. Lithium failed to inhibit aggression in any of the mice tested following acute administration of a wide range of doses (40-300mg/kg, ip). Subacute administration of lithium for 5 days, however, produced a dose related inhibition of fighting behavior, with an ED50 of 80.9mg/kg. Antiaggressive doses of lithium did not produce ataxia or significant impairment of neuromuscular coordination. It is concluded that lithium is a selective antagonist of isolation-induced aggression and may act on serotonergic mechanisms. 24 references. (Author abstract modified)

003283 Marini, James L.; Sheard, M. H. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06508 **Thyrotropin-releasing hormone (TRH): lack of effect on shock-elicited fighting (SEF) in rats.** Communications in Psychopharmacology. 2(2):139-144, 1978.

To investigate the effect of high doses of thyrotropin releasing hormone (TRH) on shock elicited fighting (SEF) in rats, male albino rats were injected with TRH. Doses of 0.125 and 0.25 mg/kg TRH had no effect on SEF 30 min. postdose, and 0.50 mg/kg TRH had no effect at 15, 30, or 45 min. postdose. At 50 mg/kg there was no significant effect of TRH on spontaneous motor activity or flinch jump levels. The results do not rule out involvement of TRH in modification of aggressive behavior by lithium and other drugs with antithyroid properties in situations where chronic administration modifies the hypothalamic pituitary thyroid axis. 14 references. (Author abstract modified)

003284 Marks, Philip C.; O'Brien, Mick; Paxinos, George. School of Psychology, University of New South Wales, Kensington, NSW 2033, Australia **Chlorimipramine inhibition of muricide: the role of the ascending 5-HT projection.** Brain Research (Amsterdam). 149(1):270-273, 1978.

The role of the ascending 5-hydroxytryptamine (5-HT) projection in the inhibition of muricide by 5-HT potentiating drugs was examined in 20 male Wistar rats. Eight of the experimental animals were intact natural mouse killers, 4 were natural mouse killers subjected to 5,7-dihydroxytryptamine (5,7-DHT) lesions of the ascending 5-HT projection, and 8 were not tested for muricide prior to surgery but killed mice following 5,7DHT lesions. The 5-HT reuptake blocker chlorimipramine (CMI) at a dose of 25mg/kg inhibited mouse killing in 6 of the 8 natural killers and in 1 of 11 lesioned animals. At 20mg/kg, CMI inhibited muricide in 5 of 8 intact animals and in 2 of 12 lesioned animals. A low dose of CMI (10mg/kg) did not significantly inhibit muricide in any group. Inhibition of muricide following CMI was not due to gross motor debilitation. It is concluded that the antimuricidal effect of CMI depends on the integrity of the ascending 5-HT projection in the rat. 24 references.

003285 Marquardt, Gerald M.; DiStefano, Victor; Ling, Lydia L. Environmental Protection Agency, Metabolic Effects Branch, OPP/CED, 401 M Street, SW, Washington, DC 20460 **Pharmacological and toxicological effects of beta-3,4-methylenedioxyamphetamine isomers.** Toxicology and Applied Pharmacology. 45(3):675-683, 1978.

The differential effects of beta-3,4-methylenedioxyamphetamine (MDA) isomers on the behavior, toxic response, and cardiovascular system of male Swiss-Webster mice were investigated. Racemic and R-MDA caused apparent hallucinogenic and amphetamine-like behavioral responses in mice. S-MDA produced no hallucinogenic behavior but was more potent than racemic or R-MDA in eliciting an amphetamine-like behavior response. S-MDA was the most toxic isomer and R-MDA the least toxic. All three isomers produced an initial pressor response in cats, which diminished in amplitude upon repeated administration; this response was blocked by phenoxybenzamine and was greatly reduced by reserpine pretreatment. The MDA isomers also potentiated the rise in blood pressure resulting from norepinephrine. These findings indicate that the MDA isomers produce initial pressor responses by an amphetamine-like action. S-MDA effects were indistinguishable from those of amphetamine. 21 references. (Author abstract modified)

003286 Marsden, C. A.; Curzon, G. Department of Neurochemistry, Institute of Neurology, Queen Square, London WC1N 3BG, England **The contribution of tryptamine to the behavioural effects of L-tryptophan in tranylcypromine-treated rats.** Psychopharmacology (Berlin). 57(1):71-76, 1978.

Male Sprague-Dawley rats pretreated with the monoamine oxidase inhibitor tranylcypromine (20mg/kg) and given L-tryptophan (50mg/kg) developed a behavioral syndrome characterized by hyperactivity, stereotypy, tremor, and hyperreactivity. Increasing the dose of L-tryptophan to 100mg/kg produced an additional small increase in locomotor activity, a striking increase in behavioral score, a small increase in brain serotonin (5-hydroxytryptamine, 5-HT) over that found after the lower dose, and a considerable increase in brain tryptamine. Tryptamine (1-5mg/kg) in combination with tranylcypromine produced behavioral effects similar to those of L-tryptophan and tranylcypromine. P-chlorophenylalanine pretreatment, which reduced brain 5-HT, prevented the behavioral effects of tryptamine. Inhibition of peripheral decarboxylase with RO4-4602 (40mg/kg) reduced brain tryptamine without altering brain 5-HT, while reducing locomotor activity and the behavioral score of rats given tranylcypromine and 100mg/kg L-tryptophan. Results indicate that 5-HT and tryptamine are both responsible for behavioral changes following treatment with tryptophan and tranylcypromine. 16 references. (Author abstract modified)

003287 Martin, James T. Faculty of Natural Sciences and Mathematics, Stockton State College, Pomona, NJ 08240 **Imprinting behavior: pituitary-adrenocortical modulation of the approach response.** Science. 200(4341):565-567, 1978.

The effects of the pituitary/adrenocortical system on imprinting behavior in newly hatched ducks were examined. Plasma corticosterone concentrations in the ducks exposed to an imprinting model were inversely related to the strength of approach behavior. Injections of corticosterone before imprinting reduced following behavior, whereas alpha1-10-adrenocorticotropin or antiserum to corticosterone augmented following behavior. It is concluded that the sensitive period for imprinting may be regulated by changes in the pituitary/adrenocortical axis. 17 references. (Author abstract modified)

003288 Martinez, Joe L., Jr.; Jensen, Robert A.; Vasquez, Beatriz J.; McGuinness, Teresa; McGaugh, James L. Dept. of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92717 **Methylene blue alters retention of in-**

hibitory avoidance responses. Physiological Psychology. 6(3):387-390, 1978.

The effects of methylene blue on retention of an inhibitory avoidance response by rats and mice were examined. The studies using mice investigated the effects of graded doses of methylene blue administered shortly before or after training. A 500mg/kg dose impaired retention in mice tested 3 days after training if administered 15 min, but not 30 or 5 min, prior to training. Further studies with rats indicate that retention was enhanced by a low dose (1.0mg/kg) administered immediately after training. Retention in rats was not affected by a 1.0mg/kg dose given 15 min before training, 6 h after training, or 15 min before testing. Results are interpreted in the light of methylene blue's actions on blood hemoglobin and carbohydrate metabolism. 13 references. (Author abstract)

003289 Mason, Stephen T. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada **Parameters of the dorsal bundle extinction effect: previous extinction experience.** Pharamcology Biochemistry and Behavior. 8(6):655-659, 1978.

Two experiments were conducted to test how depletion of forebrain noradrenaline (NA) by injection of the selective neurotoxin 6-hydroxydopamine (6-OHDA) into the fibers of the dorsal bundle alters extinction behavior in rats. Lesion of the dorsal noradrenergic bundle using 6-OHDA resulted in prolonged responding in extinction of a continuously reinforced (CRF) operant level pressing response. Experiment 1 demonstrated the dorsal bundle extinction effect (DBEE) only on the first experience of extinction. Experiment 2 further tested the effect of prior extinction experience on the DBEE using a schedule in which experience of extinction was given during the acquisition process as successive visual discrimination. Although resistance to extinction was seen the first time animals were placed in extinction, it disappeared when they were retrained on CRF and extinguished a second time. These results are discussed in the context of related demonstrations of the absence of the DBEE after partially reinforced acquisition training. 30 references. (Author abstract modified)

003290 Mason, Stephen T.; Iversen, Susan D. Psychological Laboratory, University of Cambridge, Downing Street, Cambridge, England **Central and peripheral noradrenaline and resistance to extinction.** Physiology & Behavior. 20(6):681-686, 1978.

The differential effects of central and peripheral noradrenaline (NA) depletions on the acquisition and extinction of a continuously reinforced leverpressing response were determined in male rats. Animals were treated with intracerebral stereotaxic injections of 6-hydroxydopamine (6-OHDA) into the fibers of the dorsal noradrenergic bundle when adult to destroy the central NA system, with intraperitoneal injection of 6-OHDA when adult to destroy the peripheral NA system, or with intraperitoneal injection of 6-OHDA when neonates to destroy both NA systems. Resistance to extinction of a continuously reinforced lever response for food reward was found only in the groups that suffered depletion of central NA. 35 references. (Author abstract modified)

003291 Matsui, Yoshiki; Kamioka, Toshiharu. Central Research Laboratories, Sankyo Co. Ltd., Hiromachi 1-chome Shinagawa-ku, Tokyo 140, Japan **The effects of elevating gamma-amino butyrate content in the substantia nigra on the behaviour of rats.** European Journal of Pharmacology (Amsterdam). 50(3):243-251, 1978.

The behavioral effects of bilateral injection into the substantia nigra of gabaculine, a specific inhibitor of gamma-aminobutyric acid (GABA) transaminase, were investigated in male Wistar-Imamichi rats. One day after injection, GABA was increased 11-fold in the nigra, 6-fold in the thalamus and pons-medulla, and 2-fold in pallidum. Five hours after injection, rats showed continuous sniffing and head movement. This behavior was blocked by a small dose of picrotoxin injected bilaterally into the nigra; intraperitoneal haloperidol was less effective. One day after injection, rats showed increased locomotor activity, which could be blocked by high doses of picrotoxin. On the second day after injection, GABA contents in all brain regions were less than twice the control level and behavior returned to normal. Rats with gabaculine injected into the pallidum or medulla did not show changes of behavior resembling those in rats with intranigral gabaculine injections. Striatal dopamine turnover was slightly but significantly decreased 5 hours but not 24 hours after intranigral injection with gabaculine. Results suggest that gabaculine induced sniffing and head movements are mediated by nigral GABA synapses and are independent of dopaminergic systems. 30 references. (Author abstract modified)

003292 Matsuzaki, Masaji; Spingler, Philip J.; Whitlock, Eileen G.; Misra, Anand L.; Mule, Salvatore J. Nippon Merck-Banyu Research Institute, Okazaki City, Japan **Comparative effects of cocaine and pseudococaine on EEG activities, cardiorespiratory functions, and self-administration behavior in the rhesus monkey.** Psychopharmacology (Berlin). 57(1):13-20, 1978.

The effects of cocaine and pseudococaine on the electroencephalogram (EEG), heart and respiratory rates, and self-administration behavior of rhesus monkeys were examined. An intravenous injection of cocaine (2.5and 4.0mg/kg) in the monkey produced low voltage fast waves in the EEG and behavioral hyperexcitation accompanied by marked increases in the heart and respiratory rates with mydriasis and excessive salivation. In contrast, pseudococaine produced high voltage slow waves in the EEG and behavioral depression accompanied by autonomic symptoms similar to those produced by cocaine. Both isomers were self-administered by the monkeys. During cocaine self-administration sessions, the animals showed hyperexcitation in their overall behavior, while with pseudococaine they showed almost normal behavioral responses. Results suggest that cocaine produces excitatory effects and pseudococaine inhibitory effects on EEGs and behavior. Both isomers stimulate the heart and respiratory rates. 29 references. (Author abstract modified)

003293 Matte, A. C.; Tornow, H. Department of Neurology, University Hospital Eppendorf, D-2000 Hamburg 20, Germany **Parachlorophenylalanine produces dissociated effects on aggression "emotionality" and motor activity.** Neuropharmacology (Oxford). 17(8):555-558, 1978.

Intraperitoneal administration of 350mg/kg/day-chlorophenylalanine (p-CPA), a 5-hydroxytryptamine synthesis inhibitor, changed aggressive behavior, motor activity, and emotionality of male wild mice in a series of 10 minute tests conducted on 9 consectutive days. Gross motor activity was significantly correlated with aggressive behavior, and nonaggressive fine motor activity was significantly reduced. Agonistic behavior was significantly increased, with a decrease in latent time and an increase in fighting time and gross motor activity. No qualitative behavioral changes were noted. Bolus counts were significantly increased in p-CPA treated rats and in victors (both p-CPA and saline treated), compared to counts for losers. Body weight increased after p-CPA. The dissociated effects of p-CPA on nonagressive motor activity and aggression are discussed in connection with the construct of emotionality and its postulated inverse relationship to aggression. 47 references. (Author abstract modified)

003294 Meligeni, John A.; Ledergerber, Sandra A.; McGaugh, James L. Department of Psychobiology, School of Biological

Sciences, University of California, Irvine, CA 92717 **Norepinephrine attenuation of amnesia produced by diethyldithiocarbamate.** Brain Research (Amsterdam). 149(1):155-164, 1978.

Rats given 680mg/kg diethyldithiocarbamate (DDC) approximately one half hour before training in an inhibitory avoidance task showed impaired retention performance when tested one week after training. Intracerebroventricular or subcutaneous injections of norepinephrine (NE) administered shortly after training attenuated the disruptive effects of DDC on retention performance. NE (0.01microg) administered centrally attenuated the DDC-induced retention deficit when animals were trained with a high intensity (2mA) but not a low intensity (0.5mA) footshock. The lowest dose of subcutaneously administered NE (5microg/kg) was also effective in attenuating DDC-induced retention deficits only when animals were trained with higher intensity footshock. Higher doses of NE (50microg/kg and 500microg/kg) were more effective when animals were trained with lower intensity footshock. 29 references. (Author abstract)

003295 Meliska, Charles J.; Trevor, Anthony J. Psychology Department, Monmouth College, Monmouth, IL 61462 **Differential effects of ketamine on schedule-controlled responding and motility.** Pharmacology Biochemistry and Behavior. 8(6):679-683, 1978.

The effects of ketamine injections on the response rate of rats trained to bar press for food reinforcement were studied. Ketamine significantly increased response rates of both drug naive and drug experienced rats for the first 10 minutes after injection. With larger doses of ketamine, response rates decreased significantly during the first 10 minutes after injection irrespective of prior drug experience, but increased significantly above control thereafter in drug experienced animals. Both doses of ketamine enhanced spontaneous locomotor activity significantly, irrespective of prior drug experience. These results suggest that there is no direct relationship between the effects of ketamine on motility and its effects on responding rates. Differences in the time course and dose dependency of the effects sugget that ketamine stimulates schedule controlled responding and spontaneous locomotor activity via different neuropharmacologic mechanisms. 20 references. (Author abstract modified)

003296 Mendelson, Wallace B.; Hill, Shirley Y. Bldg. 10, Room 3N224, NIH, Bethesda, MD 20014 **Effects of the acute administration of ethanol on the sleep of the rat: a dose-response study.** Pharmacology Biochemistry and Behavior. 8(6):723-726, 1978.

Seven hour sleep recordings were performed on 46-male Sprague-Dawley rats to determine the effects of intraperitoneal injections of saline or varying doses of ethanol. Total minutes of rapid eye movement (REM) sleep and percentage REM sleep were decreased in a dose dependent manner. Percentage nonREM sleep increased with progressively higher doses. The decrease in REM sleep appeared to be related to a decrease in the number of REM sleep episodes and an increase in the length of the REM/nonREM cycle. Other variables such as mean length of REM sleep episodes and REM sleep efficiency were unchanged. The data suggest that the ethanol-induced REM sleep was dose related. A lack of change was shown over the entire seven-hour recording at low dose levels and a decrease at the highest dose level. It is concluded that the data may help explain inconsistencies in the literature on the sleep patterns of normal humans. 11 references. (Author abstract modified)

003297 Mickley, G. Andrew; Teitelbaum, Herman. Physiological Psychology Division, Behavioral Sciences Department, Armed Forces Radiobiology Research Institute, Bethesda, MD 20014 **Movement induced in cataleptic rats: differential effects produced by electrical stimulation of the lateral hypothalamus, substantia nigra, and reticular formation.** Psychopharmacology (Berlin). 57(2):145-149, 1978.

The effect of electrical stimulation of various brain structures on neuroleptic produced catalepsy was studied in 18 male Sprague-Dawley rats. Stimulation of the lateral hypothalamus and, to a lesser extent, the reticular formation successfully countered haloperidol (6mg/kg) catalepsy. Stimulation of the substantia nigra produced a less significant increase in activity in haloperidol treated rats. Dissociation between behavioral arousal and cortical electroencephalogram during stimulation of the reticular formation was observed. 20 references. (Author abstract modified)

003298 Miczek, Klaus A.; O'Donnell, James M. Department of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **Intruder-evoked aggression in isolated and nonisolated mice: effects of psychomotor stimulants and L-dopa.** Psychopharmacology (Berlin). 57(1):47-55, 1978.

The effects of psychomotor stimulants and L-dopa on intruder evoked aggression in isolated and nonisolated male Swiss-Webster mice were examined. Attack and threat behavior were decreased in resident mice treated with d-amphetamine, methamphetamine, methylphenidate, cocaine, or L-dopa. Doses required to produce the antiaggressive effects were two to four times higher in mice housed singly than in group housed mice. Intruder mice treated with d-amphetamine, methamphetamine, or methylphenidate were more frequently attacked by nontreated resident opponents, escaped more often, assumed the defensive upright posture less frequently, and moved about more often. L-dopa nonspecifically decreased all elements of agonistic and nonagonistic behavior, while the amphetamines and methylphenidate suppressed attacks, increased escapes, decreased upright postures, and increased nonagonistic locomotion. The antiaggressive effects of cocaine were not accompanied by changes in other behavioral elements. 51 references. (Author abstract modified)

003299 Middaugh, Lawrence D.; Santos, Carroll A., III. Department of Biochemistry, Medical University of South Carolina, Charleston, SC 29043 **Effects of methadone on behavior maintained by fixed ratio reinforcement schedules.** Pharmacology Biochemistry and Behavior. 8(5):521-526, 1978.

The effects of subcutaneous injections of methadone hydrochloride (0.75mg/kg,1.5mg/kg, and 2.5mg/kg) on lever pressing maintained by fixed ratio schedules of reinforcement were examined in C57BL/6J and DBA/2J mice, which have been previously reported to have opposite changes in activity following injections of narcotic analgesics. Response output over a 30 minute session decreased as a function of increasing drug dose when reinforcement was delivered for every five responses. Increasing the response to reinforcement ratio from 5 to 20 in a second experiment doubled and nearly quadrupled responding by DBA and C57 mice, respectively. Injecting animals maintained on this schedule with methadone reduced responding to the same extent as that observed in the first experiment. Findings provide no support for the effect of methadone being rate dependent. It is concluded that the opposite changes in locomotor activity observed in DBA and C57 mice following exposure to narcotic analgesics do not generalize to behavior under control of reinforcing stimuli. 20 references. (Author abstract modified)

003300 Miller, Loren; Cornett, Teresa; Nallan, Gary. Veterans Administration Hospital, Cooper Drive Division, Lexington, KY 40507 **Marihuana: effect on nonverbal free recall as a func-**

tion of field dependence. Psychopharmacology (Berlin). 58(3):297-301, 1978.

The effect of marihuana on free recall of nonverbal memory was evaluated by presenting 22 male volunteers with line drawings of geometric figures for 10 acquisition trials. Each subject served as his own control. The study was performed over two sessions with drug condition and list of stimulus materials counterbalanced. Recall varied with drug condition and scores obtained on the Embedded Figures Test. Marihuana reduced recall mainly in those subjects making two or more errors on the Embedded Figures Test and had little effect on subjects making one or more errors. Intrusion errors were also elevated following marihuana intoxication, but this effect was unrelated to embedded figures performance. Results are discussed with reference to degree of field dependence and cognitive style. 27 references. (Author abstract)

003301 Misslin, R.; Ropartz, Ph.; Ungerer, A.; Mandel, P. Laboratoire de Psychophysiologie, 7, rue de l'Universite, F-67000 Strasbourg, France **Non-reproducibility of the behavioural effects induced by scotophobin.** Behavioural Processes (Amsterdam). 3(1):45-56, 1978.

Three different samples of the peptide scotophobin were tested successively on the light/dark preference test and emotional reactivity of mice. Only one of these samples gave results similar to those described by Ungar et al. (1972), that scotophobin significantly reduced the time that mice spent in the dark. No difference was found between the treated animals and the controls in the other two experiments. Results question the claims for the specificity of scotophobin in the transfer of behavioral information. 12 references. (Author abstract modified)

003302 Modrow, H. E.; Skala, K.; Bliss, D. K. Department of Psychology, Southern Illinois University, Carbondale, IL 62901 **Physiological substrates of state dependent learning.** Psychopharmacology (Berlin). 58(2):8, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the effects of disruption of neural pathways on drug dissociation was reported. In a shuttle avoidance task after injections of sodium pentobarbital or saline, animals with lesions of the amygdala, the centrum medianum nucleus of the thalamus, or the anterior polysensory cortex showed significantly more transfer to the opposite drug state than sham operated animals. Results support the hypothesis that a diffuse pathway projecting from the centrum emdianum and amygdala to the polysensory cortex mediates drug dissociation. (Author abstract modified)

003303 Moore, Mitchell S.; Thompson, Donald M. Department of Pharmacology, Georgetown University Schools of Medicine and Dentistry, 3900 Reservoir Rd. N.W., Washington DC 20007 **Acute and chronic effects of cocaine on extinction-induced aggression.** Journal of the Experimental Analysis of Behavior. 29(2):309-318, 1978.

The effect of cocaine on aggression resulting from extinction of keypecking behavior in pigeons was studied. In acute dosages of cocaine, aggressive behavior decreased without effect on keypecking behavior, but higher doses resulted in disruption of both behaviors. With chronic drug administration, some tolerance developed in the disruptive effects of cocaine on the food reinforced responding, except at the highest levels tested. No clear-cut indication of tolerance to the initial effect of cocaine on the aggressive behavior was noted at any dose. 23 references (Author abstract modified)

003304 Mormede, P.; Dantzer, R. I.N.R.A., Station de Pharmacologie-Toxicologie, 180, chemin de Tournefeuille, F-31300 Toulouse, France **Effects of dexamethasone on discriminative conditioning in pigs.** Physiology & Behavior. 21(2):279-281, 1978.

The effects of dexamethasone (DX) on discriminative fear conditioning were examined in four female and four castrated male cross-bred piglets. Animals were trained in a shuttlebox to avoid electric shocks according to a continuous avoidance schedule. After stabilization of the response rate, the pigs were submitted to discriminative Pavlovian fear conditioning. In a subsequent test session, presentation of the positive conditioned stimulus (CS) increased the avoidance response rate to a greater extent than did the negative CS. Administration of 0.2mg/kg DX before Pavlovian conditioning and before test sessions enhanced the increase in avoidance response rate to presentation of both positive and negative CS. Results suggest that DX treatment results in selective enhancement of reaction to Pavlovian stimuli rather than facilitation of the discriminatory processes involved in differentiating between two types of Pavlovian signals. 10 references. (Author abstract)

003305 Morris, Michael D.; Gebhart, G. F. Department of Psychology, Coe College, Cedar Rapids, IA 52402 **The effect of morphine on fear extinction in rats.** Psychopharmacology (Berlin). 57(3):267-271, 1978.

The effect of morphine on fear extinction was investigated in male albino rats. Animals were trained on an appetitive discrete trial discriminated punishment task in which they learned to suppress responding when an intense flashing light predicting punishment was present and to respond rapidly on trials when the flashing light was absent. Morphine (0.75, 3.0, or 6.0mg/kg) was administered prior to a fear extinction session consisting of 60 nonshocked presentations of the flashing light. Two saline control groups, one that received fear extinction and one that did not, were also included. On the day following fear extinction, all rats were tested in the undrugged state on the discriminated punishment problem, but without shock. Rats that had received 3.0and 6.0mg/kg morphine before the fear extinction session were suppressed by the flashing light more than the saline extinction group or the 0.75mg/kg morphine treatment group. The two higher dose morphine groups were suppressed as readily as the saline group that received no fear extinction. Results are attributed to the antiemotionality effects of morphine. 21 references. (Author abstract modified)

003306 Moschovakis, A.; Liakopoulos, D.; Armaganidis, A.; Kapsambelis, V.; Papanikolaou, G.; Petroulakis, G. Department of Biological Chemistry, Medical School, University of Athens, Goudi-609, Athens, Greece **Cannabis interferes with nest-building behavior in mice.** Psychopharmacology (Berlin). 58(2):181-183, 1978.

The effects of various fractions of cannabis and tobacco pyrolysis products on nest building behavior in mice were assessed. The following drugs were injected under a saline/drug/saline schedule: d-amphetamine (6mg/kg); pentobarbital (25mg/kg); delta9-tetrahydrocannabinol (THC; 10, 5, and 2.5mg/kg); the cannabis fractions designated 1S (water soluble products), 2S (nonsoluble, nonvolatile products), and 3S (fraction normally inhaled); and analogous fractions of tobacco pyrolysis. THC (10mg/kg) and the cannabis fractions 2S and 3S had the greatest disruptive effects on nest building behavior. THC (5mg/kg) and the inhalable fraction of tobacco pyrolysate also disrupted the normal behavioral pattern. Results indicate that 2S and 3S are the active fractions of cannabis pyrolysate. 15 references. (Author abstract modified)

003307 Mucha, R. F.; Niesink, R.; Kalant, H. Department of Pharmacology, University of Toronto, Toronto, Canada M5S 1A8 **Tolerance to morphine analgesia and immobility measured in**

rats by changes in log-dose-response curves. Life Sciences. 23(4):357-364, 1978.

Using the bar and tailflick tests, morphine log dose response (LDR) curves were determined for immobility and analgesia, respectively, in male Wistar rats following 15 daily intraperitoneal injections of 0, 20, or 200mg/kg morphine sulfate. The LDR curves for the two measures were qualitatively similar. Chronic morphine treatment resulted in a shift to the right and flattening of both curves. These results indicate that the flattening of the LDR curve in morphine tolerant rats is general to a number of opiate effects and raise the possibility that both morphine produced immobility and analgesia are subserved, in part, by a similar mechanism. In addition, after a test dose of 900mg/kg, more rats in the 20mg/kg than in the 200mg/kg treatment group died of convulsions. Thus, tolerance developed to lethality produced by the convulsive effects of opiates. 42 references. (Author abstract)

003308 Musty, Richard E.; Sands, Richard. Neuropsychology Laboratory, Dept. of Psychology, John Dewey Hall, University of Vermont, Burlington, VT 05401 **Effects of marijuana extract distillate and cannabidiol on variable interval performance as a function of food deprivation.** Pharmacology (Basel). 16(4):199-205, 1978.

The effects of marihuana extract distillate (MED), cannabidiol (CBD), and their combinations on variable interval (VI) performance in Wistar derived rats over a range of deprivation levels were studied. Rats were tested on VI performance at five levels of food deprivation and were treated with a vehicle control, MED at 7.5mg/kg and 11.25mg/ kg, CBD at 15mg/kg or combinations: 7.5mg/kg MED plus 15mg/kg CBD and 11.25mb/kg MED plus 15mg/kg CBD. MED produced a depression of VI performance which was greatest at low levels of deprivation. CBD did not depress performance, however when CBD was combined with MED, potentiation of depression occurred which was not additive, but occurred at high levels of deprivation. It is concluded that MED depresses performance most at low levels of deprivation, and CBD potentiates the depression produced by MED at high levels of deprivation. 24 references. (Author abstract modified)

003309 Myers, R. D. Department of Psychological Sciences, Purdue University, West Lafayette, IN 47907 **Psychopharmacology of alcohol.** Annual Review of Pharmacology and Toxicology. 18:125-144, 1978.

The factors of pharmacological significance which influence an animal's pattern of alcohol consumption in an experimental situation are examined. Coverage also is given to the effect of alcohol itself, acting as a CNS drug, upon certain processes that are mediated by cells in the brain. The mechanisms involving the central action of dopamine, norepinephrine, 5-hydroxytrptamine, and their metabolites may constitute only a fraction of the perplexing neurochemical brain activity underlying aberrant drinking behavior. When this fluid is administered acutely or taken chronically, a myriad of changes occurs in other transmitter and humoral systems in the brain. The in vivo and in vitro release of acetylcholine from the cerebral cortex and other areas of the brain, in either the anesthetized or conscious animal, are markedly suppressed by alcohol given systemically. In a rat treated with alcohol acutely or chronically, an increase in 5'-adenosine triphosphatase (ATPase) is seen in brain synaptosomes, but ATP and creatinine phosphate levels in the brain decline. Amino acids are equally affected by alcohol, and polypeptides also may be involved in this fluid's effects. 230 references. (Author abstract modified)

003310 Myslobodsky, Michael S.; Shavit, Yehuda. Psychobiology Research Unit, Department of Psychology, Tel-Aviv University, Ramat-Aviv, Israel **Hemispheric asymmetry of visual evoked potentials with motor imbalance in rats.** Brain Research (Amsterdam). 157(2):356-359, 1978.

The hemispheric asymmetry of visual evoked potentials was examined in relation to motor imbalance in freely moving female Wistar rats with epidural cortical electrodes implanted over symmetrical points of the visual cortex. Ten of 11 rats studied showed a stable symmetry of evoked potentials in the region of the slow secondary negative wave. Following intraperitoneal injection of 1.25mg/kg d-amphetamine, rats rotated away from the hemisphere with the smaller secondary evoked potential and the higher dopamine concentration. These electrophysiological findings are discussed in terms of the biochemical asymmetry of the rat brain. 12 references.

003311 Nagayama, Haruo; Takagi, Akinori; Nakamura, Eitoku; Yoshida, Hideo; Takahashi, Ryo. Department of Neuropsychiatry, Nagasaki University School of Medicine, 7-1 Sakamoto-Machi, Nagasaki 852, Japan **Circadian susceptibility rhythm to apomorphine in the brain.** Communications in Psychopharmacology. 2(4):301-310, 1978.

The mechanism of the circadian fluctuation of the effect of neuroleptics was investigated in male Sprague-Dawley rats housed under controlled conditions with a daily period of artificial light from 19:30 to 7:30 and darkness for the other 12 hours. Apomorphine induced stereotypy showed circadian fluctuation in these animals, with the most pronounced effect when apomorhpine was administered at 19:30 and the least noticeable effect when the drug was given at 13:30, regardless of the amount of apomorphine administered. When intracerebral concentration of apomorphine was estimated in rats given the drug at different times, no differences were found. Results suggest a circadian susceptibility rhythm of the dopamine receptors in the brain. 21 references. (Author abstract modified)

003312 Naik, S. R.; Kelkar, M. R.; Sheth, U. K. Pharmacological Research Unit, CSIR, Department of Pharmacology, Seth G. S. Medical College, Parel, Bombay-400012, India **Attenuation of stereotyped behaviour by sex steroids.** Psychopharmacology (Berlin). 57(2):211-214, 1978.

The effects of the sex steroids testosterone, progesterone, and estradiol on stereotyped behavior induced by beta-phenylethylamine (PEA) and amphetamine were studied in normal, castrated, and ovariectomized mice. PEA increased stereotyped behavior in castrated and ovariectomized mice. Pretreatment with sex steroids attenuated stereotypy induced by PEA in normal, castrated, and ovariectomized mice. Pretreatment with sex steroids also significantly inhibited stereotyped behavior induced by amphetamine but failed to alter increased motor activity caused by amphetamine or PEA. The possible effect of sex steroids on stereotyped behavior through changes in central neurotransmitters is discussed. 18 references. (Author abstract modified)

003313 Nakajima, Shinshu. Department of Psychology. Dalhousie University, Halifax, Nova Scotia, Canada **Attenuation of amnesia by hydrocortisone in the mouse.** Physiology & Behavior. 20(5):607-611, 1978.

The effects of hydrocortisone on the retrograde amnesia produced by eletroconvulsive shock (ECS) were studied in 228 Charles River, CD-1 mice. The animals were given ECS after one trial training in a step through apparatus and tested for passive avoidance behavior 7 days later. The amnesic effect of ECS was found to be absent in the animals that were injected with hydrocortisone prior to the administration of ECS. Hydrocortisone alone, without ECS, had no significant effect on passive

avoidance. There was no indication that the hormone suppressed ECS-induced seizure activity in the brain. Results suggest that hydrocortisone protects animals from amnesia by acting on the brain before the onset of the disruptive action of ECS. 15 references. (Author abstract)

003314 Nance, Dwight M.; Gorski, Roger A. Department of Anatomy, College of Medicine, University of South Florida, Tampa, FL 33612 **Similar effects of estrogen and lateral hypothalamic lesions on feeding behavior of female rats.** Brain Research Bulletin. 3(5):549-553, 1978.

The interaction of lateral hypothalamic (LH) lesions with the behavioral effects of estrogen on feeding behavior and bodyweight were examined in female Sprague-Dawley rats. Relative to sham operated controls, rats with small LH lesions showed a transitory period of anorexia and initial weight loss. Food intake and weight gains of lesioned animals subsequently returned to control levels, although a small chronic reduction in mean bodyweight was observed. Daily changes in food intake and weight during 4 day estrous cycle as well as postovariectomy increases in food intake and weight were comparable for control and lesioned animals. Both groups showed a similar decrease in food intake and weight following subcutaneous injection of estradiol benzoate (EB). LH animals showed an exaggerated diurnal distribution of meals, ate smaller meals of shorter duration, and had larger intervals between meals during the light period. EB shifted the feeding patterns of sham operated animals toward the meal patterns showed by the lesioned rats. Lesioned rats also showed a normal change in feeding patterns following EB. Results indicate that LH lesions and EB have similar and perhaps additive effects on the feeding behavior of female rats. 17 references. (Author abstract modified)

003315 Nasello, Antonia G.; Ramirez, Oscar A. Departamento de Farmacologia, Facultad de Ciencias Quimicas, Universidad Nacional de Cordoba, Cordoba, Argentina **Open-field and Lashley III maze behaviour of the offspring of amphetamine-treated rats.** Psychopharmacology (Berlin). 58(2):171-173, 1978.

The open field and maze behavior of the offspring of amphetamine treated albino Wistar rats was examined. Rats were given 0.5mg/kg d,l-amphetamine sulphate or saline once daily throughout gestation, beginning on day 1 of pregnancy. When adult, the offspring of amphetamine treated mothers had higher motor activity in the open-field test, as measured by locomotion and rearing. In a Lashley III maze, the treated group made more errors than controls in the first 4 days. Ater day 4, no differences in number of errors or running time were observed between the two groups. Results are discussed in terms of brain catecholamine metabolism. 16 references. (Author abstract modified)

003316 Neill, Darryl B.; Herndon, James G., Jr. Department of Psychology, Emory University, Atlanta, GA 30322 **Anatomical specificity within rat striatum for the dopaminergic modulation of DRL responding and activity.** Brain Research. 153(3):529-538, 1978.

Experiments were conducted to test the hypothesis that the effect of a striatal neurotransmitter on behavior depends on the striatal subregion in which the transmitter is released. The direct application of microgram quantities of crystalline dopamine (DA), d-amphetamine, or scopolomine to the ventral anterior of the neostriatum of rats decreased response efficiency on a differential reinforcement of low rate (DRL) 10sec schedule of reinforcement. Similar applications to the dorsal globus pallidus or posterior striatum either did not alter or increased response efficiency. A comparison of dose response functions for injections of DA in solution into ventral anterior, central and posterior striatum confirmed that only injections into ventral anterior striatum decreased response efficiency on the DRL schedule. The same striatal map was found for the DA-induced increase in spontaneous locomotor activity in tilt boxes. It is concluded that dopaminergic transmission in ventral anterior striatum, in contrast to the other striatal and pallidal sites tested, is involved in the modulation of behavioral arousal. 27 references. (Author abstract modified)

003317 Nielson, H. C.; DeWitt, J. R.; Gill, J. H. Department of Psychology, University of Utah, Salt Lake City, UT 84112 **Some failures of the drug discrimination hypothesis of state-dependent learning.** Psychopharmacology (Berlin). 58(2):8, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, two experiments that fail to support the drug discrimination hypothesis of state dependent learning were reported. Rats were fed in the drugged state for 45 days, then in a runway either drugged or nondurgged for an additional 28 days to make feeding and mazerunning state dependent. When drug conditions were reversed during 12 more days, latencies to reach food and actual food consumption were uncorrelated and showed dissociation. In a second experiment, nondrugged cats were trained to perform foreleg flexion avoidance responses to direct electrical stimulation of the brain and to tone. Doses of pentobarbital, meprobamate, chlordiazepoxide, and chloral hydrate that abolished responses elicited by tone had no effect on responses elicited by central stimulation. Cats under doses of pentobarbital that produce state dependent learning learned to respond to central stimulation but not to peripheral stimulation. It is concluded that drugs limit the stimuli that can be used in learning and performing conditioning respones, rather than producing stimuli that control responding. (Author abstract modified)

003318 Niemegeers, C. J. E.; Colpaert, F. C. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **The effects of haloperidol on discriminative responding controlled by the cocaine cue.** Psychopharmacology (Berlin). 58(2):8, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, an analysis of the effects of 0.16mg/kg haloperidol on the stimulus generalization gradient of cocaine (0.31-10mg/kg) in rats was presented. Animals were trained to discriminate 10mg/kg cocaine from saline in a discrete trial, two lever, food reinforced drug discrimination procedure. Haloperidol produced a shift to the right in cocaine's stimulus generalization gradient, caused some increase in the accuracy of selection, retarded lever selection, decreased total response output, and attenuated the percentage of responding on the selected lever. Implications of these findings for studies of the effects of neuroleptics on internal cues produced by CNS stimulant drugs were discussed. (Author abstract modified)

003319 Nistico, Giuseppe; Rotiroti, Domenicantonio; De Sarro, Angela; Stephenson, John D. Institute of Pharmacology, Faculty of Medicine, Piazza XX Settembre 4, I-98100 Messina, Italy **Behavioural, electrocortical and body temperature effects after intracerebral infusion of TRH in fowls.** European Journal of Pharmacology (Amsterdam). 50(3):253-260, 1978.

Intracerebroventricular injection of 0.25-5mcg thyrotropin releasing hormone (THR) in Rhode Island Red fowls produced intense behavioral stimulation, electrocortical desynchronization, and a slight increase in body temperature. An intense pattern of stereotyped head/neck movements, increase in locomotor activity, repeated pecking and preening, vocalization, erection of tail feathers, and occasional escape responses was observed. This

syndrome lasted for about 30 minutes and was followed by slight behavioral sedation with attentuated stereotypy. Similar increases in locomotor activity and stereotypy were evoked by infusing TRH into the hypothalamus. Unilateral infusion of TRH into the nucleus basalis or nucleus mesencephalicus profundus (homologous to the mammalian striatum and substantia nigra, respectively) produced intense stereotyped head/neck movements, wet dog shakes, and vocalization. Injection of TRH into hyperstriatum, neostriatum, olfactory ventricle, eminentia basalis, or lateral part of the mesencephalon had no effect on behavior and body temperature. The effects of intraventricular TRH were antagonized by pretreatment with haloperidol or spiperone, but not by nonadrenergic or serotonergic antagonists. The behavioral effects of TRH were independent of its endocrine properties, since they were not observed after systemic or intracerebroventricular injection of thyrotropin, thyroxine, and triiodothyronine. 45 references. (Author abstract modified)

003320 Nomura, Yasuyuki; Segawa, Tomio. Dept. of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Hiroshima 734, Japan **Muscarinic hyposensitivity in the developing rat pretreated with 6-hydroxydopa.** European Journal of Pharmacology (Amsterdam). 50(4):431-435, 1978.

Atropine induced locomotor stimulation was examined in developing Wistar rats that had been treated with 6-hydroxydopa at birth. Atropine induced locomotor stimulation was first observed on day 20 and gradually increased with age. Treatment with 6-hydroxydopa potentiated atropine induced locomotor stimulation on days later than day 20 and inhibited pilocarpine induced catalepsy on day 30. This suggests that central cholinergic neurons, probably in the neostriatum, reach functional maturity between 15 and 20 days and that pretreatment with 6-hydroxydopa induced muscarinic hyposensitivity in the developing rat. 10 references. (Author abstract modified)

003321 Oei, T. P. S.; Singer, G. Department of Psychology, La Trobe University, Bundoora, Victoria 3083, Australia **Schedule-induced self-injection of nicotine, methadone and heroin by naive animals.** Psychopharmacology (Berlin). 58(2):9, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of schedule-induced self-injection of nicotine, methadone, and heroin was reported. Rats were randomly allocated to the drug groups under conditions of normal and reduced body weight and with or without a 60 second fixed interval food delivery schedule. Animals self-injected significantly more methadone and heroin, but not nicotine, than saline. For all three drugs, the highest self injection rate was seen in animals in the 80% reduced body weight and fixed interval food delivery schedule groups. At normal body weight and without a food delivery schedule, animals injected more heroin than any of the other drugs. Results indicate that there is an interaction of pharmacological and environmental factors that maximize drug self-injection and that this pattern differs for the three drugs tested.

003322 Oei, Tian P.; Ng, Chee P. Department of Psychology, La Trobe University, Bundoora, Victoria 3083, Australia **6-Hydroxydopamine-induced catecholamine depletion and passive avoidance learning in rats.** Pharmacology Biochemistry and Behavior. 8(5):553-556, 1978.

Rats were injected with 6-hydroxydopamine either intracisternally, intraperitoneally, or both to determine the effects of central and peripheral catecholamine depletion on a step down passive avoidance task. All rats acquired the response at the end of five acquisition trials, but the rates of acquisition for the drug treated groups were significantly different from that of the control group. No significant difference in performance was observed between groups during the extinction period. Plasma corticosterone levels in rats depleted of central or peripheral catecholamine did not differ significantly from each other after passive avoidance training. Findings indicate that an intact central orperipheral catecholaminergic system may not be necessary for the acquisition and extinction of a step down passive avoidance response. 22 references. (Author abstract modified)

003323 Oke, Arvin Floyd. University of Kansas **Schizophrenic-like tendencies in rats neonatally treated with 6-hydroxydopamine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arobr, MI, Univ. M-films, No. 78-9374, HC$15. MF$7.50. 101 p. 1977.

Two experiments are presented which investigate the assumption that the adult rat, following neonatal depletion of brain catecholamines with 6-hydroxydopamine (6-OHDA), shows a more pronounced disruption of a learned response when confronted with irrelevant visual stimuli. The 6-OHDA treated group showed equivalent and at times superior performance on a T-maze for simple black and white discrimination until competitive irrelevant stimuli were introduced, when the performance of the 6-OHDA group shifted to a level significantly poorer than that of the control group. In a replication of the first experiment using a water maze, two of three patterns of irrelevant stimuli consecutively presented produced significant decrements in performance. When discrete areas of each brain were analyzed for catecholamine content, depletion of norepinephrine in the hippocampus was found to be most predictive of performance disruption during presentations of irrelevant stimuli. Results are taken to enhance the viability of this animal model as a prototype of the human schizophrenic condition, which reflects an inability to exclude irrelevant material. (Journal abstract modified)

003324 Olianas, Maria C.; De Montis, Graziella M.; Concu, Alberto; Tagliamonte, Alessandro; Di Chiara, Gaetano. University of Cagliari, Via Porcell 4, I-09100 Cagliari, Italy **Intranigral kainic acid: evidence for nigral non-dopaminergic neurons controlling posture and behavior in a manner opposite to the dopaminergic ones.** European Journal of Pharmacology (Amsterdam). 49(3):223-232, 1978.

The unilateral, intranigral administration of kainic acid (KA) to male Sprague-Dawley rats produced a syndrome characterized by early sequelae of contralateral and ipsilateral circling and by chronic contralateral turning associated with moderate loss of neurons in the pars reticulata. The acute contralateral turning seemed to be related to dopaminergic nigroneostriatal neuron stimulation, since it was prevented by previous intranigral injections of 6-hydroxydopamine. The acute ipsilateral circling and chronic contrateral turning, on the other hand, appeared to be independent of the integrity of the dopaminergic system and may be due to an initial stimulation, followed by destruction of a nigral neuronal system that mediates turning behavior in a manner opposite to that of nigrostriatal dopamine (DA). Treatment with d-amphetamine or apomorphine changed the contralateral turning into ipsilateral turning, while haloperidol potentiated the contralateral turning. Bilateral injection of KA into the nigra resulted in chronic stereotyped sniffing and gnawing, which were not inhibited by haloperidol. Moreover, haloperidol did not produce catalepsy in these animals. It is suggested that intranigral KA infection destroyed a neuronal system antagonistic to DA and resulted in reduction of the response to DA receptor stimulation of the corpus striatum. 25 references. (Author abstract)

003325 Olianas, Maria C.; De Montis, Graziella M.; Mulas, Giorgio; Tagliamonte, Alessandro. University of Cagliari, Via

Porcell 4, I-09100 Cagliari, Italy **The striatal dopaminergic function is mediated by the inhibition of a nigral, non-dopaminergic neuronal system via a strio-nigral GABAergic pathway.** European Journal of Pharmacology (Amsterdam). 49(3):233-241, 1978.

The unilateral, intranigral administration of muscimol in male Sprague-Dawley rats produced spontaneous contralateral circling, lasting from 90 minutes to several hours, according to the dose (5, 25, or 50ng). This contralateral circling was potentiated by 0.2mg/kg haloperidol and antagonized by 1mg/kg apomorphine. Bilateral injection of muscimol into the substantia nigra resulted in stereotyped movements which were resistant to haloperidol administration. Haloperidol (up to 5mg/kg) also failed to produce catalepsy in these bilaterally injected rats. Unilateral intranigral injection of 20ng picrotoxin produced ipsilateral turning, which was potentiated by 0.2mg/kg subcutaneous apomorphine and antagonized by haloperidol injected in the contralateral striatum. Bilateral injection of the same dose of picrotoxin induced rigid catalepsy, which was not sensitive to apomorphine treatment. The contralateral turning and stereotypies induced by acute, intranigral injection of muscimol were similar to the chronic effects of intranigral kainic acid (KA), while the effects of intranigral picrotoxin were similar to the acute effects of KA. It is suggested that nigral, KA sensitive neurons control posture in manner opposite to striatal dopamine and that the function of the nigrostriatal dopaminergic system is to inhibit these neurons by activating a strionigral gama-aminobutyric acid (GABAergic) containing pathway. 24 references. (Author abstract modified)

003326 Overstreet, David H.; Dubas, George. School of Biological Sciences, Flinders University of South Australia, Bedford Park, South Australia 5042, Australia **Tolerance to the behavioural effects of physostigmine in rats: lack of importance of behavioural compensation.** Communications in Psychopharmacology. 2(2):93-98, 1978.

To investigate the relative importance of development of behavioral and pharmacological tolerance, male Hooded-Wistar rats performing an operant response for water reward were injected with physostigmine before or after the operant task. Partial tolerance development to the response suppressing effect of physostigmine was exhibited regardless of whether they were treated chronically before or after the operant task. A similar, but less marked, partial tolerance developed to the hypothermic effects of physostigmine. Physostigmine tolerant animals were not less sensitive to the behavioral effects of pilocarpine. These results suggest that pharmacological tolerance is a more important determinant of the tolerance development than is behavioral compensation, and that a reduction in the sensitivity of cholinergic receptors may not be an important mechanism underlying tolerance to physostigmine. 19 references. (Author abstract modified)

003327 Paglietti, E.; Quarantotti, B. Pellegrini; Mereu, G.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Italy **Apomorphine and L-dopa lower ejaculation threshold in the male rat.** Physiology & Behavior. 20(5):559-562, 1978.

The subcutaneous administration of apomorphine (50 mcg/kg) to sexually experienced Sprague-Dawley male rats decreased the number of penile intromissions necessary to reach ejaculation and accelerated the achievement of ejaculation. Similar results were obtained with the intraperitoneal administration of L-dopa (100mg/kg) in animals pretreated with Ro4-4602, a peripherally acting carboxylase inhibitor. The effect of apomorphine was prevented by pimozide (250 mcg/kg), a specific inhibitor of dopamine receptors. Results suggest that dopaminergic hyperactivity may be involved in premature ejaculation. 16 references. (Author abstract)

003328 Palfai, Tibor; Brown, Oliver M.; Walsh, Thomas J. Psychology Department, Syracuse University, Skytop Laboratories, M-15, Syracuse, NY 13210 **Catecholamine levels in the whole brain and the probability of memory formation are not related.** Pharmacology Biochemistry and Behavior. 8(6):717-721, 1978.

The time and dose related effects of reserpine, an amnesia producing, drug, on retention and catecholamine levels in the whole brain were studied in two experiments to determine the probability of amnesia and the levels of the neurotransmitters dopamine (DA) and norepinephrine (NE). Amnesia was induced with reserpine or was blocked with L-dopa and 5-hydroxytryptophan before or after passive avoidance training in mice. The levels of DA and NE in the whole brain were measured in corresponding groups with gas chromatography/mass spectrometry. The results indicate a time and dose dependent effect of reserpine on retention and the levels of whole brain catecholamines. However, no correlation appears to exist between the behavioral and biochemical effects of the drug. The implication is that the levels of whole brain catecholamines during training do not predict subsequent retention performance. If catecholamines are involved in memory, then their functional availability in the brain, rather than their overall levels would be important. 28 references. (Author abstract modified)

003329 Paul, Linda; Diaz, Jaime; Bailey, Beva. Department of Psychology, University of California, Los Angeles, CA 90024 **Behavioral effects of chronic narcotic antagonist administration to infant rats.** Neuropharmacology (Oxford). 17(8):655-657, 1978.

Male Wistar rats pups were given daily subcutaneous injections of the opiate antagonist naltrexone throughout infancy. Chronic naltrexone treatment did not appear to alter the ontogeny of reflex behavior and body growth in these animals. However, the latency to morphine induced analgesia was shorter in naltrexone treated pups than in controls 9 days after the last injection of naltrexone. 6 references. (Author abstract modified)

003330 Pettibone, Douglas J.; Kaufman, Nathan; Scally, Michael C.; Meyer, Edwin, Jr.; Ulus, Ismael; Lytle, Loy D. Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Striatal nondopaminergic neurons: possible involvement in feeding and drinking behavior.** Science. 200(4346):1175-1177, 1978.

In a study of the possible involvement in feeding and drinking behavior of striatal nondopaminergic neurons, intracaudate injections of kainic acid destroyed striatal neurons containing acetylcholine and gamma-aminobutyric acid (GABA), but left dopaminergic nerve terminals in this brain region intact. Rats injected with the drug are aphagic and adipsic, and have other behavioral abnormalities strikingly similar to those seen in animals with lesions in the dopaminergic nigrostriatal bundle. Since kainic acid appears to destroy only neurons whose cell bodies, but not axons or terminals, are in close proximity to the injection site, it is concluded that the behavioral impairments seen in these animals are the result of damage to neurons that may normally be directly or indirectly innervated by nigrostriatal dopaminergic nerves. 13 references. (Author abstract modified)

003331 Pfister, William R.; Noland, Vicki; Lowy, Martin T.; Nichols, David E.; Yim, George K. W. Department of Pharmacology, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN 47907 **Comparison of the behavioral effects of para-chloroamphetamine, chlordimeform, quipazine, and intraventricular serotonin in the rat.** Communications in Psychopharmacology. 2(4):287-296, 1978.

Male Sprague-Dawley rats given 5mg/kg parachloroamphetamine (PCA) exhibited the "serotonergic syn-

drome," characterized by forepaw treading, head weaving, hindlimb abduction, rigidity, Straub tail, and tremor. The pesticide chlordimeform (CDM, 80mg/kg), a moderate inhibitor of nonamine oxidase that raises brain 5-hydroxytryptamine (5-HT) levels, also induced the syndrome. Both PCA and CDM induced additional symptoms including backing, circling, hyperactivity, hyperreactivity, and hyperreflexia. Both 5-HT antagonists, cinanserin and methysergide, were effective in blocking various components of the behavioral effects elicited by PCA or CDM. Intraventricular 5-HT and the direct 5-HT agonists quipazine failed to elicit the serotonergic syndrome in rats, even in lethal doses. These results suggest that the "serotonergic syndrome" is not mediated solely by an increase in serotonergic transmission. 15 references. (Author abstract)

003332 Poling, Alan; Simmons, Mark A.; Appel, James B. Behavioral Pharmacology Laboratory, Department of Psychology, University of South Carolina, Columbia, SC 29208 **Morphine and shock detection: effects on shock intensity.** Communications in Psychopharmacology. 2(4):333-336, 1978

The effects of morphine (2.5-20mg/kg) on shock detection were investigated in Sprague-Dawley rats trained to detect 0.05mA or 0.02mA electric shocks in a discrete trial, two choice discrimination procedure. In animals trained at the 0.05mA intensity, morphine produced dose dependent decreases in correct discriminations during trials when shock was present. Morphine failed to significantly affect discrimination during shock and nonshock trials in animals trained at the 0.02mA intensity. These findings emphasize the importance of situational factors in determining drug induced perceptual changes. 6 references. (Author abstract)

003333 Puech, Alain J.; Simon, Pierre; Boissier, Jacques R. Faculte de Medecine Pitie-Salpetriere, Departement de Pharmacologie, 91, boulevard de l'Hopital, F75634, Paris Cedex 13, France **Benzamides and classical neuroleptics: comparison of their actions using 6 apomorphine-induced effects.** European Journal of Pharmacology (Amsterdam). 50(4):291-300, 1978.

The effects of six benzamides and eight classical neuroleptics on six apomorphine induced behaviors were investigated in male Swiss NMRI mice and Wistar rats. Results suggest that some apomorphine induced effects (stereotyped behavior, circling, climbing, and increased motor activity) were related to stimulation of postsynaptic dopaminergic receptors, while other effects (hypothermia and decreased activity) appeared to be related to presynaptic dopaminergic receptors. Pimozide, sulpiride, thioproperazine, GRI-1665, and TER-1546 selectively blocked presynaptic dopaminergic receptors, at least within the dose range used. Clozapine, chlorpromazine, levomepromazine, and thioridazine selectively blocked postsynaptic receptors. Haloperidol, metoclopramide, prochlorperazine, sultopride, and tiapride were not selective for either type of receptor. 28 references. (Author abstract modified)

003334 Quinton, Elton E. Dept. of Psychology, University of Louisville, Louisville, KY 40208 **Subamnesic cycloheximide treatment delays consolidation in mice.** Journal of Comparative and Physiological Psychology. 92(4):742-748, 1978.

The effects of administration of cycloheximide (CYC) on learning and memory were investigated in mice. In Experiment 1, groups of C57 BL/6J mice were given passive avoidance training and then administered different doses of cycloheximide immediately, 30 min, or 1 hr after training. In Experiment 2, mice were given a nonamnesic administration of CYC or saline immediately after training and another injection of CYC or saline 1 hr after training. Results of these and other experiments indicate that the administration of a nonamnesic dose of CYC immediately after training renders the memory susceptible to disruption by additional doses of CYC or other amnesic treatments for a longer period of time than normal. It is suggested that CYC delays consolidation and prolongs the labile period of memory formation. 11 references. (Author abstract modified)

003335 Ramaekers, F.; Rigter, H.; Leonard, B. E. Department of Biochemistry, University of Nijmegen, Nijmegen, Netherlands **Parallel changes in behavior and hippocampal monoamine metabolism in rats after administration of ACTH-analogues.** Pharmacology, Biochemistry and Behavior. 8(5):547-551, 1978.

The effects of adrenocorticotrophic hormone (ACTH) analogues on hippocampal serotonin metabolism and passive avoidance behavior were examined in rats. Application of a footshock during the aquisition trial of a one trial passive avoidance test was associated with a rise in the concentratio of serotonin in the hippocampi of rats 24 hours after the trial; this rise in hippocampal serotonin was abolished by amnesic treatment with carbon dioxide immediately after footshock. ACTH 4-10 and ACTH 4-10 (7D-Phe) alleviated the carbon dioxide-induced amnesia for the passive avoidance response when administered 1 hour before a retrieval test 24 hours after acquisition, but did not have an antiamnesic effect when given before acquisition. The antiamnesic effect of ACTH 4-10 and ACTH 4-10 (7D-Phe) was correlated with a rise in hippocampal serotonin concentration similar to that observed in nonamnesic animals. ACTH 11-24 had no amnesic effects and no effect on hippocampal serotonin. Changes in the hippocampal concentrations of noradrenaline, dopamine, tryptophan, and tyrosine were not related to behavioral activity of any of the peptides. Alterations in hippocampal serotonin metabolism 24 hours after acquisition of a passive avoidance response appear to be associated with the retrievability of the response. 19 references. (Author abstract modified)

003336 Ray, Donald; Nagy, Z. Michael. Department of Psychology, Marshall University, Huntington, WV 25701 **Emerging cholinergic mechanisms and ontogeny of response inhibition in the mouse.** Journal of Comparative and Physiological Psychology. 92(2):335-349, 1978.

Three experiments designed to determine 1) the generality of the cholinergic inhibitory model, 2) the nature of the onset of the cholinergic inhibitory function, and 3) the extent to which cholingeric agents might affect the acquisition of a passive avoidance response (PAR) by immature subjects, are presented. The centrally active anticholinergic scopolamine produced a dose dependent evaluation in locomotor activity in 19-day-old and adult mice. Acquisition and retention of a step off PAR was initially studied in nondrugged subjects. Mice as young as 7 days of age learned and retained the PAR for 1 hr. Twenty four hour savings, however, were not observed until 19 days of age. Simple PAR performance deficits following scopolamine injection were first seen at 15 days of age. Mice in those age groups exhibiting 24 hr retention (19-day-olds and adults) were used to assess carryover effects of scopolamine on retest. Only in the case of juveniles did scopolamine, injected prior to training, disrupt 24 hr retest performance. Since methylscopolamine, a peripherally active anticholinergic, had no effect on activity and PAR performance, it is assumed that scopolamine's effects were of central origin. The results suggest that behavioral suppression comes under cholinergic control during the second and third postnatal weeks but that cholinergic control during the second and third postnatal weeks but the cholinergic mechanisms may not mediate response inhibition uniformly throughout development. 31 references. (Author abstract modified)

003337 Riley, Anthony L.; Zellner, Debra A. Dept. of Psychology, American University, Washington, DC 20016 **Methyl-**

phenidate-induced conditioned taste aversions: an index of toxicity. Physiological Psychology. 6(3):354-358, 1978.

The effectiveness of methylphenidate to condition food aversions was examined in groups of rats who were injected with various doses of methylphenidate hydrochloride after consumption of saccharin. Small aversions were found after one conditioning trial, with repeated saccharin/methylphenidate pairings resulting in continued decrements in consumption. The strength of the aversion as well as the amount of individual variability were dose related, with weaker aversions and greater variability occurring at the smaller dose (15mg/kg). Although aversions were quite pronounced at higher doses, individual variability, although small, was still evident. The similarities and differences between methylphenidate induced aversions and aversions based on emetics are discussed, along with the implications of these results as indices for methylphenidate induced toxicity. 37 references. (Author abstract)

003338 Riley, Edward P.; Lochry, Elizabeth A.; Freed, Earl X. Department of Psychology, State University of New York at Albany, Albany, NY 12222 **Differential tolerance to pentobarbital in rats bred for differences in alcohol sensitivity.** Psychopharmacology (Berlin). 58(2):167-170, 1978.

Two lines of rats bred for differences in motor impairment following alcohol treatment were tested to see if they were also differentially affected by drugs that are cross-tolerant with alcohol. Alcohol sensitive animals showed a decrement in stabilimeter activity at doses of 8 and 16mg/kg pentobarbital. Alcohol insensitive animals were affected only by the higher dose of pentobarbital, and the resulting impairment was less than that of the alcohol sensitive group. Following a dose of 18mg/kg pentobarbital, alcohol sensitive animals were more likely to lose their righting reflex, and alcohol insensitive animals slept longer. Results indicate that the differential sensitivity shown by these animals is not specific to alcohol, but can be generalized to another depressant. 12 references. (Author abstract modified)

003339 Roberge, A. G.; Roy, J.-P.; Boisvert, C. Departement de Biochimie, Faculte de Medecine, Universite Laval, Quebec G1K 7P4, Canada **Effect of metergoline, p-chlorophenylalanine and dopa on delayed response in cats and the relationship between the mesolimbic and nigrostriatal neurons.** Psychopharmacology (Berlin). 58(2):9, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the role of neurotransmitters in delayed response performance was reported. Acute or chronic injection of 250mg/kg p-chlorophenylalanine (PCPA) and 14mcg/kg metergoline (MTGL) did not significantly disturb delayed response performance in cats. A significant increase in response latencies was observed in cats treated with PCPA alone, but not in cats treated with only MTGL. Administration of L-dopa and L-5-hydroxytryptophan did not alter delayed response performance but did increase response latencies in a dose dependent fashion. MTGL (14mcg/kg/day) administered during the first 10 days of training significantly decreased response latencies without significantly affecting the number of errors. The improved performance was correlated with increased dopamine levels in limbic structures and decreased serotonin content in all brain structures. Results suggest that serotonergic pathways exert an inhibtory influence on areas like the mesolimbic system that retain high concentrations of dopamine.

003340 Roberts, Peter J.; Sharif, Najam A. School of Biochemical and Physiological Sciences, University of Southampton, Southampton S09 3TU, England **Effects of L-glutamate and related amino acids upon the release of (3H)dopamine from rat striatal slices.** Brain Research (Amsterdam). 157(2):391-395, 1978.

The effects of L-glutamate and related amino acids on the release of (3H)dopamine (DA) from striatal slices from female Wistar rats were investigated. L-glutamate, D-glutamate, L-aspartate, and DL-homocysteic acid were all able to effect release of accumulated (3H)DA from the striatal slices in a calcium dependent manner. Inclusion of glutamic acid diethylester in the medium had no effect on the spontaneous release of (3H)DA, but did antagonize the glutamate stimulated release of (3H)DA. These results suggest that specific glutamate receptors may be involved in regulating DA release in the striatum. 22 references.

003341 Robertson, Ann; Mogenson, Gordon J. University of Western Ontario, Ontario, Canada **Evidence for a role for dopamine in self-stimulation of the nucleus accumbens of the rat.** Canadian Journal of Psychology (Toronto). 32(2):67-76, 1978.

The effects of centrally administered spiroperidol, a dopamine receptor blocking agent, on self-stimulation of the nucleus accumbens and medial prefrontal cortex were investigated in male albino rats. Self-stimulation of the nucleus accumbens was not changed by microinjections of spiroperidol into the ipsilateral or contralateral prefrontal cortex. Similarly, self-stimulation of the prefrontal cortex was not altered by microinjections of spiroperidol into the nucleus accumbens. By controlling for nonspecific effects of spiroperidol, the results provide further evidence that dopaminergic neurons contribute to self-stimulation of the nucelus accumbens. 38 references. (Author abstract modified)

003342 Rodgers, R. J.; Semple, J. M. Postgraduate School of Psychology, University of Bradford, Bradford, England **Pituitary-adrenocortical axis and shock-induced fighting in rats.** Physiology & Behavior. 20(5):533-537, 1978.

Pituitary/adrenocortical influences on shock-induced fighting were studied in Sprague-Dawley rats. Results show that adrenalectomy, hypophysectomy, or a high dose (12.5IU) of adrenocorticotropic hormone (ACTH) suppressed fighting behavior, while hydrocortisone or a low dose (6.25 IU) of ACTH augmented the response. None of these hormonal manipulations were found to significantly alter shock thresholds. Results are discussed in relation to known influences of pituitary/adrenal secretions on fear motivated behaviors and limbic system activity. 53 references. (Author abstract modified)

003343 Roffman, M.; Bernard, P. S.; Dawson, K. M.; Sobiski, R. E.; Saelens, J. K. Research Department, Pharmaceuticals Division, Ciba-Geigy Corporation, Summit, NJ 07901 **The effects of haloperidol and clozapine on circling induced by electrical stimulation of the substantia nigra and the ventromedial tegmentum.** Neuropharmacology (Oxford). 17(11):943-946, 1978.

Circling behavior was induced in male CRW rats by electrical stimulation of the zona compacta of the substantia nigra and the ventromedial tegmentum, which contain the A9 and A10 dopaminergic cell bodies whose terminals end in the corpus striatum and mesolimbic areas, respectively. The behavioral pattern of circling differed, depending on which area was stimulated. Although differing in potency, systemically administered haloperidol and clozapine equally attenuated circling induced by stimulation of the two areas. The similar sensitivities of the two areas to these antipsychotic agents suggest that this model does not distinguish between agents with high (haloperidol) and low (clozapine) extrapyramidal syndrome liability in man. 18 references. (Author abstract modified)

003344 Rogers, Joseph Brown. University of California, San Diego **Cholinergic conductance as a component of mnemonic**

processes. (Ph.D. dissertation). Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 78-13152 HC$15. MF$7.50. 126 p. 1978.

The cholinergic agents physostigmine, scopolamine, and alpha-neurotoxin were used to test the hypothesis that changes in cholinergic conductance are essential components in memory processes. Data obtained from rats demonstrated that strength of memory may be manipulated by three variables: the setting of a functional range of cholinergic conductance by administration of cholinergic agents at the time of learning, elevation or depression of cholinergic conductance by administration of the agents at time of recall testing, or the amount of time allowed between learning and recall testing. A neuropharmacological model of the mnemonic process was developed from the data, and its predictive value was contrasted against that of other nonassociative theories of cholinergic drugs and memory. The model suggests and successfully predicts the results of experiments using complex schedules of drug administration at many different training/retest intervals. These experiments suggest that cholinergic drug state dependence is an artifact of fortuitously chosen, short training/retest intervals. Studies were also conducted on the preliminary pharmacological localization of cholinergic pathways involved in memory. (Journal abstract modified)

003345 Rowland, Neil. Department of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Effects of insulin and 2-deoxy-D-glucose on feeding in hamsters and gerbils.** Physiology & Behavior. 21(3):291-294, 1978.

Golden hamsters (Mesocricetus auratus) and gerbils (Meriones unguiculatus) increased their food intake and rate of weight gain in response to daily injections of protamine zinc insulin. Both species showed modest and delayed increases of food intake after acute insulin injections, despite severe hypoglycemia. Neither species increased its feeding after 2-deoxy-D-glucose. Results are discussed in terms of the relevance of glucoprivation to normal feeding and possible hormonal abnormalities in hamsters. 31 references. (Author abstract)

003346 Roy, S. N.; Bhattacharyya, A. K.; Pradhan, Sikta; Pradhan, S. N. Department of Pharmacology, Howard University College of Medicine, Washington, DC 20059 **Behavioural and neurochemical effects of repeated administration of cocaine in rats.** Neuropharmacology (Oxford). 17(8):559-564, 1978.

The effects of repeated intraperitoneal injections of cocaine (15mg/kg, twice daily at 8 hour intervals) on spontaneous motor activity (SMA), stereotypy (ST), and neurotransmitter levels in various brain areas were investigated in male Wistar derived Walter Reed rats. Following repeated injections of cocaine, SMA and ST gradually increased up to day 9 and then gradually decreased to days 18-20. Concomitantly, the dopamine (DA) level in the caudate nucleus (CN) and diencephalon/midbrain (DM) increased and the 5-hydroxytryptamine (5-HT) level in the DM and pons/medulla (PM) decreased, reaching their maximum or minimum levels on day 9; these levels gradually returned to normal by day 18 and remained so up to day 30. Slight changes in norepinephrine and acetylcholine levels were also observed. It is concluded that changes in behavior induced by repeated cocaine administration can be roughly correlated with changes in the DA level in the CN and 5-HT levels in the DM and PM. 27 references. (Author abstract modified)

003347 Sahakian, B. J.; Koob, G. F. Laboratory of Neuroendocrine Regulation, Department of Nutrition and Food Science, M.I.T., Cambridge, MA 02139 **The relationship between pipradrol-induced responding for electrical brain stimulation, stereotyped behaviour and locomotor activity.** Neuropharmacology (Oxford). 17(6):363-366, 1978.

Rats with lateral hypothalamic electrodes were treated with 0, 5, 10, and 15mg/kg pipradrol in a Latin square design. Barpressing for electrical stimulation of the brain increased in a dose dependent fashion. A second group of rats was treated with pipradrol in a similar test paradigm in which locomotor activity and stereotyped behavior were measured. Stereotyped behavior induced by pipradrol showed the same dose related increase as the rate of responding for brain stimulation. However, stimulation of locomotor activity by pipradrol followed an inverted U-shaped function, with a decrease at 15mg/kg pipradrol, probably as a result of response competition. Results are discussed in terms of the reward enhancing effect of psychomotor stimulant drugs and the blending of stereotypy into a learned response sequence. 25 references. (Author abstract)

003348 Sahgal, Arjun; Iversen, Susan D. Department of Psychology, Downing Street, Cambridge CB2 3EN, England **The effects of chlordiazepoxide on a delayed pair comparison task in pigeons.** Psychopharmacology (Berlin). 59(1):57-64, 1978.

The effects of chlordiazepoxide on a delayed pair comparison task in pigeons were studied. Five pigeons were successfully taught a variation of the Konorski delayed pair comparison task, using a red or green stimulus. The bird was required to respond to the left or right hand key, depending on whether the two successively presented center key stimuli were the same (left) or different (right). Delay intervals ranged from zero to 9 seconds, and stable performance decrements with increasing delay were obtained. Intramuscular administration of chlordiazepoxide disrupted performance at doses greater than 4 mg/kg. All delays were affected. Results are discussed in terms of encoding and attention. 53 references. (Author abstract modified)

003349 Sanger, D. J. Department of Psychology, University College, P.O. Box 78, Cardiff CF1 1XL, Wales **Effects of d-amphetamine on temporal and spatial discrimination in rats.** Psychopharmacology (Berlin). 58(2):185-188, 1978.

The effects of amphetamine on both temporal and spatial discrimination were examined in three male hooded rats. Rats were trained to lever-press for food reinforcers on a multiple schedule with a fixed-interval (FI) and a differential reinforcement of low rate (DRL) component. Illumination of a stimulus light above the right lever indicated that responses on that lever would be reinforced on a FI 60 second schedule, while responses on the left lever were without programmed consequences. When the light above the left lever was illuminated, responses on that lever were reinforced on a DRL 15 second schedule. Amphetamine (0.25, 0.5, 1.0, and 2.0mg/kg) was administered after behavior had been brought under schedule control. As doses of amphetamine increased, performance tended towards a constant high rate of responding on the right lever, with a much lower response on the left lever. Results emphasize that behavioral effects of drugs depend not only on patterns of ongoing behavior, but also on the context in which this behavior occurs. 24 references. (Author abstract modified)

003350 Sanger, D. J. Department of Psychology, University College, PO Box 78, Cardiff, CF1 1XL, Wales **The effects of d-amphetamine and scopolamine on drinking induced by a multiple schedule.** Psychopharmacology (Berlin). 58(3):311-315, 1978.

The effects of d-amphetamine and scopolamine (both drugs at doses of 0.25, 0.5, 1.0, and 2.0mg/kf) on drinking induced by a multiple fixed time, fixed interval schedule were examined in three male hooded rats. Both drugs increased rates of lever-pressing at lower doses and reduced levels of licking and water intake at all doses. The pattern of fixed interval lever-pressing

was altered by both drugs, with increases in the proportion of responses emitted during early parts of the intervals. Amphetamine increased the proportion of licks occurring in the early segments of the interfood intervals, while scopolamine had variable effects on licking patterns. There were no consistent differences in the effects of the drugs on licking induced by the two schedules. 29 references. (Author abstract modified)

003351 Sansone, Mario. Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R., via Reno 1, I-00198 Rome, Italy **Facilitating effects of chlordiazepoxide on locomotor activity and avoidance behaviour of reserpinized mice.** Psychopharmacology (Berlin). 59(2):157-160, 1978.

The effects of chlordiazepoxide on locomotor activity and avoidance behavior were investigated in resperpinized mice. Results indicate that chlordiazepoxide increases the spontaneous locomotor activity of both normal and reserpinized mice and facilitates the avoidance behavior of mice pretreated with reserpine. These effects of chlordiazepoxide on reserpinized animals were unexpected, as they are usually associated with amphetamines and antidepressant drugs. 28 references. (Author abstract)

003352 Sansone, Mario. Laboratorio di Psicobiologia e Psicofarmacologia C.N.R., via Reno n. 1, I-00198 Rome, Italy **Effects of chlordiazepoxide, amitriptyline, imipramine, and their combinations on avoidance behaviour in mice.** Psychopharmacology (Berlin). 59(2):151-155, 1978.

Chlordiazepoxide, imipramine, and amitriptyline, given alone or in combination, were tested in mice subjected to five daily 100 trial avoidance sessions in a shuttlebox. When the drugs were given alone, chlordiazepoxide and the lower doses of imipramine facilitated avoidance behavior, while the higher doses of the two antidepressants impaired avoidance behavior. Combinations of chlordiazepoxide and imipramine produced some facilitating effects, while depressant effects prevailed with the chlordiazepoxide/amitriptyline combinations. 25 references. (Author abstract)

003353 Sansone, Mario; Renzi, Paolo. Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R., 1 via Reno, I-00198 Rome, Italy **Facilitating effects of chlordiazepoxide on the performance of mice in an inhibitory avoidance task.** Psychopharmacology (Berlin). 59(2):161-163, 1978.

The effects of chlordiazepoxide on inhibitory avoidance behavior were investigated in mice, using an automated procedure. Animals were subjected to five 15 minute sessions. Facilitation of inhibitory avoidance behavior was observed following the administration of chlordiazepoxide at doses that did not produce significant effects on spontaneous locomotor activity. 12 references. (Author abstract)

003354 Schechter, Martin D. Department of Pharmacology, Eastern Virginia Medical School, P.O. Box 1980, Norfolk, VA 23507 **Lack of blockade of central dopaminergic receptors by narcotics: comparison with chlorpromazine.** European Journal of Pharmacology (Amsterdam). 49(3):279-284, 1978.

The ability of morphine and fentanyl to produce amphetamine-like responding in male Sprague-Dawley rats trained to discriminate a low dose (0.6mg/kg) of d-amphetamine was investigated. Administration of morphine (2.5, 5.0, and 7.5mg/kg) or fentanyl (0.02 and 0.04mg/kg) produced saline appropriate responses in the food rewarded, two choice operant procedure. Pretreatment with morphine and fentanyl had no significant effect on the d-amphetamine induced discriminative stimulus. In contrast, 1.25 and 2.5mg/kg chlorpromazine antagonized d-amphetamine discrimination. Results indicate that despite their similar effects on brain dopamine turnover, morphine and fentanyl do not act on the same receptor sites as the neuroleptics; i.e.,they probably do not block brain dopamine receptors. 33 references. (Author abstract modified)

003355 Schnare, Sharon N.; Lenzer, Irmingard I. Saint Mary's University, San Antonio, TX 78284 **Effects of sodium phenobarbital on brain stimulation behavior, behavioral seizures, and EEG seizure activity.** Psychological Reports. 42(3):1007-1016, 1978.

The effects of sodium phenobarbital on behavior reinforced by electrical stimulation of the brain, behavioral seizures, and EEG seizure activity were observed in seven male Sprague-Dawley rats. The rate of response on the placebo day was compared to the rate of response on the drug day. An increase in response on the drug day over the placebo day was called a positive phenobarbital effect, a decrease a negative phenobarbital effect. For some animals the positive phenobarbital effect disappeared when the animal's rate of response was calculated for seizure free time, i.e.,when the time spent in seizure was subtracted from the reinforcement session. For other animals, the phenobarbital effect, whether positive or negative, was not directly related to time gained on the drug day compared to the placebo day. A new concept of seizure proneness, measured by the number and duration of seizures and spike after discharges, is proposed. Significant correlations were found for seizure proneness and phenobarbital effect. 15 references. (Author abstract modified)

003356 Schultz, W.; Ungerstedt, U. Institut de Physiologie de l'Universite, CH-1700 Fribourg, Switzerland **Striatal cell supersensitivity to apomorphine in dopamine-lesioned rats correlated to behaviour.** Neuropharmacology (Oxford). 17(6):349-353, 1978.

The sensitivity of glutamate excited striatal cells to subcutaneous, systemic injections of apomorphine was measured in unlesioned rats and in rats with 3-17-month-old unilateral lesions of the dopaminergic nigrostriatal pathway resulting from a stereotaxic injection of 6-hydroxydopamine into the ascending bundle of dopamine axons. The lowest doses effective in depressing striatal cell activity were used to determine the sensitivity to apomorphine. These were 0.1-0.4mg/kg in unlesioned animals and 0.005 and 0.01mg/kg in denervated animals; there was a 10-80 fold increase in striatal cell sensitivity to apomorphine after dopamine lesions. The cellular effects were comparable in sensitivity and time course to the rotational behavior of the animals as recorded in a rotometer. 29 references. (Author abstract)

003357 Scrollini, F.; Pizzi, A.; Amigoni, S. Zambeletti Research Laboratory, Via Zambeletti, I-20021 Milan, Italy **The psychopharmacological properties of pinazepam, a new benzodiazepine derivative.** Arzneimittel-Forschung (Aulendorf). 28(3):423-426, 1978.

The pharmacological differences between the behavioral effects of a new benzodiazepine derivative, 7-chloro-1-propargyl-5-phenyl-3H-1, 4-benzodiazepin-2-one (pinazepam) and diazepam were investigated in rats. Pinazepam was more than twice as active as diazepam at a dose range between 1.25mg/kg and 10mg/kg in reducing the conditioned emotional response. Pretreatment with pinazepam at doses of 2.5mg/kg and 5.0mg/kg partially prevented the disruption of the avoidance responses induced by inverting the conditioned stimulus. On the other hand, pinazepam was less active than diazepam in reducing the number of avoidance responses in a conditioned avoidance situation. Neither pinazepam nor diazepam disrupted the conditioned responses in a fixed interval operant behavior. 12 references. (Author abstract)

003358 Shearman, G.; Lal, H. Department of Pharmacology and Toxicology, College of Pharmacy, University of Rhode

Island, Kingston, RI 02881 **Differential responding controlled by the discriminative stimuli produced by convulsant drugs in the rat.** Psychopharmacology (Berlin). 58(2):10, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of discriminative stimuli produced by convulsant drugs was reported. Male rats were trained to respond for food reinforcement on a lever on one side of a food cup following a subconvulsive dose (20mg/kg) of pentylentrazol (PTZ) and to respond on a lever on the alternate side following saline injection. Criterion was reached in 29 trials. Following PTZ in doses of 20, 10, 5, and Omg/kg, 100, 50, 28, and 0% of the subjects selected the PTZ lever. After bemegride in doses of 2.5and 5.0mg/kg, 50 and 100% of the rats selected the PTZ lever. Chlordiazepoxide antagonized the discriminative stimulus of PTZ in a dose dependent manner (median effective dose, 1.39mg/kg); d-amphetamine (0.64mg/kg) failed to generalize to PTZ. It was concluded that subconvulsive brain states can produce discriminative stimuli that are blocked by benzodiazepines.

003359 Silverman, P. B.; Ho, B. T. Texas Research Institute of Mental Sciences, 1300 Moursund Avenue, Houston, TX 77030 **Stimulus properties of DOM: commonality with other hallucinogens.** Psychopharmacology (Berlin). 58(2):10, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the stimulus properties of 2,5-dimethoxy-4-methylamphetamine (DOM) was reported. Rats were trained to discriminate saline from 0.75 and 0.5mg/kg DOM in a two lever operant procedure, with food reinforcement on a fixed ratio 20 schedule. Pretreatment with the serotonin antagonist cinanserin (5.0mg/kg) blocked the stimulus provided by DOM, without affecting saline performance. Administration of low doses of d-amphetamine, delta9-tetrahydrocannabinol, or phencyclidine resulted in predominantly saline appropriate responses, while higher doses of these compounds eliminated responding altogether. Administration of 2,5-demethoxy-4-ethylamphetamine (DOET), lysergic acid diethylamide (LSD), mescaline, or psilocybin resulted in a majority of responses on the lever paired with DOM in training. The generalization produced by DOET, LSD, mescaline, and psilocybin was abolished by cinanserin pretreatment. Results suggest that these compounds produce their discriminable effects by action at a common receptor site.

003360 Simon, Neal G.; Gandelman, Ronald. Department of Psychology, Busch Campus, Rutgers University, New Brunswick, NJ 08903 **Aggression-promoting and aggression-eliciting properties of estrogen in male mice.** Physiology & Behavior. 21(2):161-164, 1978.

The influence of estradiol benzoate (EB) on aggression was investigated in Rockland-Swiss mice. When given daily to gonadectomized adult male mice, EB induced attack behavior toward stimulus males at a level similar to that observed to intact males or castrate males treated with testosterone propionate (TP). In a second experiment, significantly fewer gonadectomized/olfactory bulbectomized males given EB were attacked by adult males, as compared to similarly prepared TP treated or intact/olfactory bulbectomized males. It is concluded that EB is as effective as TP in promoting aggression, but is less effective in eliciting fighting. 20 references. (Author abstract modified)

003361 Simpson, John B.; Epstein, Alan N.; Camardo, Joseph S., Jr. Institute of Neurological Sciences and Department of Biology, University of Pennsylvania, Philadelphia, PA 19104 **Localization of receptors for the dipsogenic action of angiotensin II in the subfornical organ of rat.** Journal of Comparative and Physiological Psychology. 92(4):581-608, 1978.

The proposal of the subfornical organ (SFO) as a site of receptors for drinking induced by angiotensin II (A-II) was investigated with several mutually confirmatory experiments. Intracranial injections of physiological doses of A-II elicited drinking if and only if applied directly to the SFO (Experiment 1). Ablation of the SFO selectively (Experiment 2) and permanently (Experiment 4) eliminated drinking elicited by physiological doses of intravenously infused A-II. Animals in which SFO had been ablated responded normally to cellular dehydration but reduced responding to the extracellular thirst of beta-adrenergic activation and hyperoncotic colloid dialysis (Experiment 3). Infusion of saralasin, an A-II antagonist, directly into the SFO selectively and reversibly antagonized intravenous A-II drinking (Experiment 5). The hypothesis that the SFO contains dipsogenic receptors for circulating A-II is strongly supported. 69 references. (Author abstract)

003362 Smith, Robert C.; Leelavathi, D.E.; Lauritzen, Ann Marie. Texas Research Institute of Mental Sciences, 1300 Moursund, Houston, TX 77030 **Behavioral effects of dopamine agonists increase with age.** Commmunications in Psycholpharmacology. 2(1):39-43, 1978

The effects of a directly acting dopamine agonist, apomorphine, and an indirectly acting dopamine agonist, d-amphetamine, on the sterotyped behavior of rats of different ages were investigated. The results indiacate that the effects of dopamine agonists are age related. Rats 20 months old showed the greatest drug effect and 2-month-old rats the least effect, with 10-month-old rats generally intermediate. The 2-month-old rates the longest persistence of this drug effect. It is concluded that changes in receptor sensitivity or drug metabolism may mediate these effects. 15 references. (Author abstract modified)

003363 Smotherman, W. P.; Levine, S. Department of Psychology, Oregon State University, Corvallis, OR 97331 **ACTH effects on response suppression and plasma corticosterone in the mouse.** Physiology & Behavior. 20(5):503-507, 1978.

The effects of adrenocorticotropin (ACTH) on behavioral and adrenocortical responses in the BALB/C mouse were investigated. ACTH was found to facilitate the suppression of activity in a situation where activity was punished by footshock. Repeated injections of ACTH were found to result in an increase in adrenocortical responsiveness. Results demonstrate the cross-species generality of effects on aversively motivated behavior. 17 references. (Author abstract modified)

003364 Soubrie, P.; Thiebot, M. H.; Simon, P.; Boissier, J. R. Unite de Neuropsychopharmacologie, U. 19 INSERM. 2, Rue d'Alesia, F-75014, Paris, France **Benzodiazepines and behavioral effects of reward (water) omission in the rat.** Psychopharmacology (Berlin). 59(1):95-100, 1978.

The effects of benzodiazepines on response suppression and drive stimulation induced by nonreward were studied in male Wistar rats. Rats deprived of water in an enclosure where they normally drank showed enhanced drinking when water was available 30 minutes later; drinking time varied with the length of the water omission session, the motivational state of the animals, and the previous number of water omission sessions. Intraperitoneal administration of diazepam, chlordiazepoxide, lorazepam, or meprobamate 30 minutes prior to the water omission session increased the time spent licking the empty bottles but failed to abolish the enhanced drinking during the subsequent water available session. It is proposed that either minor tranquilizers are devoid of general antifrustration activity or nonreward-induced frustration and nonreward-induced drive enhancement may not be correlated. 17 references. (Author abstract modified)

003365 Spealman, Roger D.; Katz, Jonathan L.; Witkin, Jeffrey M. Harvard Medical School, New England Regional Primate Research Center, 1 Pine Hill Drive, Southborough, MA 01772 **Drug effects on responding maintained by stimulus-reinforcer and response-reinforcer contingencies.** Journal of the Experimental Analysis of Behavior. 30(2):187-196, 1978.

The effects of pentobarbital and d-amphetamine were assessed on key pecking pigeons under single key multiple schedules and under two key multiple schedules in which discriminative stimuli appeared on one key while pecks on a second key produced food. A 60 sec. variable interval schedule operated on one component of each multiple schedule; either extinction or a 60 sec. variable time schedule operated in the alternate component. When the alternate component was extinction, a high rate of responding was maintained in the variable interval component of the single key schedule; responding on both keys was maintained in the variable interval component of the two key schedule. Pentobarbital increased responding in the variable interval component of the single key schedule, and increased stimulus key, but not constant key, responding in that component of the two key schedule. When the alternate component schedule was changed to variable time, responding declined in the variable interval component of the single key schedule, and stimulus key responding was no longer maintained on the two key schedule. Pentobarbital decreased responding in the variable interval component of both schedules. With an exception, d-amphetamine only decreased responding in the variable interval component of the single and two key schedules both when the alternate component schedule was extinction and when it was variable time. Results suggest that pentobarbital, but not d-amphetamine effects depend on the nature of the contingency that maintains responding. 23 references. (Author abstract modified)

003366 Sperk, Gunther; Stewart, R. Malcolm; Campbell, Alexander; Baldessarini, Ross J. Mailman Laboratories for Psychiatric Research, McLean Division of Massachusetts General Hospital, Boston, MA **Inhibition of 5,7-dhydroxytryptamine-induced supersensitivity to 5-hydroxytryptophan in mice by treatment with cycloheximide.** Brain Research (Amsterdam). 159(1):183-194, 1978.

A study was conducted to determine: 1) if cyclopheximide, a commonly employed inhibitor of protein synthesis, would inhibit development of the increased sensitivity to serotonin after destruction of presynaptic serotonin containing neurons, and 2) if such an effect of cycloheximide is due to its specific effects on protein synthesis or its toxicity. Intracisternal injection of 5,7-dihydroxytryptamine (5,7-DHT) following treatment with desmethylimipramine induced development of behavioral supersensitivity to the intraperitoneally administered serotonin precursor 5-hydroxytryptophan (5-HTP) in adult male mice. This behavior syndrome, characterized by tremor and muscle twitches, showed a clear dose/response relationship with 5,7-DHT as well as with 5-HTP. Mice lesioned with a low dose of 5,7-DHT (20mcg) were treated repeatedly with cycloheximide (45mg/kg, subcutaneously, every 12 hours for up to 10 days); this treatment resulted in a reversible decrease of cerebral protein synthesis varying between 70 and 20% with time between treatments. The myoclonic response to 5-HTP in animals pretreated with 5,7-DHT and by cycloheximide showed a decrease in intensity within 24 hours. Cycloheximide also exerted a similar, though smaller, effect following full development of sensitivity to 5-HTP over 10 days. These effects may be mediated by inhibition of rapidly turning over serotonin receptor proteins. 26 references. (Author abstract modified)

003367 Stolerman, I. P.; Pilcher, C. W. T.; D'Mello, G. D. Medical Research Council Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **Aversive properties of narcotic antagonists in rats.** Neuropharmacology (Oxford). 17(6):427, 1978.

It was hypothesized that if endogenous morphine-like substances such as enkephalin have physiological functions, narcotic antagonists would have effects in vivo even in the absence of exogenous narcotic agonists. The narcotic antagonist naloxone was paired with flavored solutions in drinking rats. Initially, only very weak taste aversions were conditioned even after four pairings of flavors with 10mg/kg naloxone. The interval between contact with the flavor and onset of drug effects was then reduced, and sensitivity to naloxone was greatly increased; the threshold dose became 1mg/kg and clear aversions were conditioned at 3.2and 10mg/kg. Findings suggest that enkephalins or related substances may be involved in the mediation of states of reward or aversion. 8 references.

003368 Stoof, J. C.; Dijkstra, H.; Hillegers, J. P. M. Department of Pharmacology, Free University, Medical Faculty, Van der Boechorststraat 7, Amsterdam-1081, The Netherlands **Changes in the behavioral response to a novel environment following lesioning of the central dopaminergic system in rat pups.** Psychopharmacology (Berlin). 57(2):163-166, 1978.

During the third week of life, a hyperactive period for the laboratory rat, the occurrence of eight categories of behavior was recorded for individual littermates transferred to a novel environment. Neonatal destruction of the catecholaminergic system by intraventricular injection of 6-hydroxydopamine (6-OH-DA) resulted in increased motor activity during the third week of life. Selective lesioning of the dopaminergic system by the combined treatment of 6-OH-DA and desmethylimipramine also induced a significant increase in some active behavioral categories. In contrast to the gross behavioral sequence of locomotion and rearing, grooming, sitting, and lying down seen in controls, the lesioned aninals showed a prolonged phase of restless locomotion. Results suggest that rats are unable to habituate adequately to a novel environment after neonatal lesioning of the dopaminergic system. 10 references. (Author abstract)

003369 Stutz, R. M.; Maroli, A. Department of Psychology, University of Cincinnati, Cincinnati, OH 45221 **Central mechanisms of reward and the narcotic cue.** Psychopharmacology (Berlin). 58(2):10, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, studies of the interoceptive cue properties of positively reinforcing brain stimulation were reviewed in relation to the centrally mediated narcotic cue. Available evidence suggests that the subjective effects of narcotics may be mediated by arousal of the systems that mediate intracranial self-stimulation (ICS). Preliminary findings of studies of the generalization of the narcotic cue to the perceptual properties of ICS and of the effects of morphine on the cue properties of ICS were presented.

003370 Swanson, Heidi H.; Norman, Mary E. Department of Anatomy, Medical School, University of Birmingham, Birmingham, England **Central and peripheral action of testosterone propionate on scent gland morphology and marking behaviour in the Mongolian gerbil.** Behavioural Processes (Amsterdam). 3(1):9-19, 1978.

Scent gland size and activity and frequency of marking under standard conditions were compared in five groups of male and female gerbils: 1) intact, sham operated controls; 2) intact with scent glands excised; 3) gonadectomized; 4) gonadectomized injected with a high dose of testosterone propionate (TP) on alternate days; and 5) gonadectomized with a low dose TP applied topically to the ventral scent gland on alternate days. The animals were housed in individual cages and tested for marking in

an open field arena with plastic pegs. The scent gland is not required in either sex for the behavioral act of marking. Topical application of a dose of TP too low to exert a systemic effect restored the scent gland but not marking. Injection of sufficient TP to restore seminal vesicle weight restored marking, as well as the scent glands. It is concluded that in the male, both marking behavior and scent gland size are controlled by the testes. The effect of androgens on marking was mediated directly through the central nervous system, and not through peripheral stimulation of the glands. Females had smaller glands and marked less than males. The ovaries appeared to have little control over marking frequency, and some control over scent gland size. It is concluded that it is possible to stimulate marking behavior to supernormal levels by TP injection, but not by topical application. 37 references. (Author abstract)

003371 Swedberg, M. D. B.; Loman, P.; Jarbe, T. U. C. University of Uppsala, Department of Psychology, P. O. Box 227, S-75104 Uppsala, Sweden **Effects of chlormethiazole (Heminevrin) on drug discrimination and open-field behavior in gerbils.** Psychopharmacology (Berlin). 59(2):165-170, 1978.

The effects of chlormethiazole (CMZ, 80mg/kg) on drug discrimination and open-field behavior were examined in adult male gerbils. Animals were trained to escape electric shock in a T-maze using CMZ as the discriminative stimulus. Substitution tests with pentobarbital (5-25mg/kg) and ethanol (0.5-2.5g/kg) indicated at least a partial similarity to the stimulus effects of CMZ, but animals could be trained to discriminate CMZ from ethanol. The CMZ stimulus was attenuated by 30mg/kg of the analeptic bemegride. Bemegride also counteracted the depressive effects of CMZ in the initial stages of open-field testing. 27 references. (Author abstract modified)

003372 Switzman, L.; Amit, Z.; White, N.; Fishman, B. Centre for Research on Drug Dependence, Psychology Department, Concordia University, Montreal, Canada **Reinforcing and aversive properties of the narcotic cue.** Psychopharmacology (Berlin). 58(2):11, 1978

At The First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the reinforcing and aversive properties of the narcotic cue was presented. Food deprived rats ran down an alley into a goal box where a novel tasting food was available. After eating the food, the rats were injected with morphine or Ringer's solution. The morphine group ran faster (displaying positive reinforcement) and ate less food (showing a conditioned taste aversion, or CTA) than the Ringer's group. Running speed for animals in which morphine produced CTA was significantly faster than running in controls. No difference in running speed was observed between the control group and animals with no CTA. Diminished food intake was not a function of nonspecific morphine effects on food consumption, as no decrease was observed in unflavored food intake. Results suggest that the discriminative stimulus properties of morphine that produce CTA are in some way related to those that produce an increase in running speed.

003373 Tagashira, Eijiro; Izumi, Tomoko; Yanaura, Saizo. Department of Pharmacology, Hoshi College of Pharmacy, Tokyo, Japan **Experimental barbiturate dependence. I. Barbiturate dependence development in rats by drug-admixed food (DAF) method.** Psychopharmacology (Berlin). 57(2):137-144, 1978.

Rats received phenobarbital or barbital admixed food on a graded increase dosage schedule for 30 to 40 days. During the medication period, animals showed signs of mild to moderate central nervous system depression, including systemic muscle relaxation, motor incoordination, staggering gait, and ptosis. Within 24 to 48 hours after withdrawal of either drug, all six animals showed abstinence symptoms, including muscle fasciculation, nuchal twitching, vocalization, increased irritability, ataxia, hyperthermia, and clonic/tonic and grand-mal seizures The withdrawal symptoms were closely correlated with the magnitude of weight loss during withdrawal. Results suggest that rats are suitable animals for tests in early stages of dependence and that the administration of drug admixed food is a useful method of developing dependence on barbiturate drugs. 22 references. (Author abstract modified)

003374 Takagi, Hiroshi; Satoh, Masamichi; Akaike, Akinori; Shibata, Takashi; Yajima, Haruaki; Ogawa, Hiroshi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto 606, Japan **Analgesia by enkephalins injected into the nucleus reticularis gigantocellularis of rat medulla oblongata.** European Journal of Pharmacology (Amsterdam). 49(1):113-116, 1978.

The degree of analgesia produced by injection of enkephalins into rat brains was investigated. Methionine-enkephalin and leucine-enkephalin produced a dose related and naloxone antagonizable analgesia in the tail pinch test, when microinjected into the nucleus reticularis gigantocellularis and nucleus reticularis paragigantocellularis of the medulla oblongata of the rat. The median analgesic doses were 1.4and 4.8mcg/rat for methionine and leucine-enkephalin, respectively. The possibility that the endogenous enkephalins play a part as pain control substances or modulators in these nuclei is discussed. 10 references. (Author abstract modified)

003375 Tanner, Trevor. Applied Pharmacology Laboratories, Welsh School of Pharmacy, University of Wales Institute of Science and Technology, Cardiff CF1 3NU, Wales **Circling behaviour in the rat following unilateral injections of p-chlorophenylalanine and ethanolamine-0-sulphate into the substantia nigra.** Journal of Pharmacy and Pharmacology (London). 30(3):158-161, 1978.

Male albino Wistar rats were observed following the unilateral intranigral injection of the gamma-aminobutyric acid (GABA) transaminase inhibitor ethanolamine-O-sulphate (EOS) or the tryptophan hydroxylase inhibitor p-chlorophenylalanine (pCPA) for spontaneous circling behavior and for circling induced by apomorphine administration. Rats injected with EOS (25-100 micrograms) exhibited spontaneous contralateral rotation for up to 3 hours after injection, while those given pCPA (25-100 micrograms) showed only a slight ipsilateral postural asymmetry. Apomorphine (1mg/kg) given 24 hours after pretreatment with EOS-induced ipsilateral circling behavior that peaked at 24 hours; in rats pretreated with pCPA, the rotation induced by apomorphine was maintained for up to 28 days. Elevated striatal concentrations of the dopamine metabolite, homovanillic acid, were observed in rats treated with either EOS or pCPA. It is proposed that GABA and 5-hydroxytryptamine may be closely related in modifying the nigrostriatal impulse flow. 23 references. (Author abstract modified)

003376 Tepper, Patricia; Woods, James H. 1110 Oxford House, Nashville, TN 37212 **Changes in locomotor activity and naloxone-induced jumping in mice produced by WIN 35,197-2 (ethylketazocine) and morphine.** Psychopharmacology (Berlin). 58(2):125-129, 1978.

The effects of ethylketazocine (EKZ), morphine, and cocaine on locomotor activity and naloxone-induced jumping were examined in female Swiss-Webster mice. Acute intraperitoneal administration of morphine or cocaine produced increases in locomotor activity that were maximal at 32-100mg/kg for morphine and 32mg/kg for cocaine. EKZ produced dose dependent de-

creases in locomotor activity from 3.2-32mg/kg. Chronic administration of EKZ led to a 6-10 fold shift to the right in the locomotor activity decreasing effect of the drug, but EKZ tolerant mice retained their sensitivity to the locomotor stimulant effects of morphine and cocaine. Acute administration of EKZ failed to sensitize mice to naloxone-induced jumping. Chronic administration of EKZ did lead to sensitivity to naloxone, but EKZ was much less efficacious in this regard than morphine. These behavioral effects of EKZ may be helpful in the classification of modes of action of different narcotic agonists. 10 references. (Author abstract)

003377 Thomas, Gary S.; Caccamise, Donna J.; Clark, Dennis L. Department of Psychology, University of Arizona, Tucson, AZ 85721 **Aggression increase and water competition decrease in squirrel monkeys given physostigmine injections.** Pharmacology Biochemistry and Behavior. 8(6):633-639, 1978.

Six adult squirrel monkeys were tested in pairs for the effects of physostigmine injections on social dominance in a water competition task. Dominance was defined by two methods: 1) number and direction of aggressive responses, and 2) successful water competition as assessed by latency to the water bottle, latency to accumulate 15 seconds of drinking, and total drinking duration. Monkeys were assigned to pairs on a "round robin" basis so that each monkey was paired with all other monkeys under control, saline, and three levels of physostigmine sulfate doses. Under drug conditions only one member of each pair was drugged. The number of aggressive responses varied as a function of the physostigmine injections. Both drinking duration and general motor activity decreased with increasing dose level of physostigmine. The nondrugged partners of drugged monkeys accumulated drinking time faster and drank more with large physostigmine doses than under control and saline conditions. It is concluded that physostigmine results in an aggression increase and a water competition decrease. 26 references. Author abstract modified.

003378 Todzy, I.; Coper, H.; Fernandes, M. Institute of Neuropsychopharmacology, Free University Berlin, Ulmenallee 30, D-1000 Berlin 19, Germany **Interaction between d-amphetamine and ethanol with respect to locomotion, stereotypies, ethanol sleeping time, and the kinetics of drug elimination.** Psychopharmacology (Berlin). 59(2):143-149, 1978.

The interaction of d-amphetamine and ethanol with respect to locomotor activity, stereotyped behavior, and sleeping time was investigated in adult male Wistar rats. Intraperitoneal administration of ethanol (0.8g/kg i.p.)enhanced and prolonged locomotor activity induced by subcutaneous injection of d-amphetamine (1mg/kg). The increased motility induced by 5mg/kg d-amphetamine was not enhanced by oral or intraperitoneal ethanol but was slightly prolonged. Stereotyped head and paw movements and licking were distinctly strengthened and protracted by 3.2g/kg oral ethanol. The modified d-amphetamine motility and stereotypies were attributed to alcohol induced prolongation of the life of d-amphetamine, resulting from inhibited d-amphetamine p-hydroxylation in the liver. Sleeping time was 153 minutes after 3.2g/kg intraperitoneal ethanol and 84 minutes after simulutaneous administration of ethanol and 5mg/kg subcutaneous d-amphetamine; the reduction in sleeping time reflects central antagonism of the two drugs. 20 references. (Author abstract modified)

003379 Tremblay, Evelyne C.; Jacob, Joseph J. Service de Pharmacologie del 'Institut Pasteur, 28, rue du Dr. Roux, F-75724 Paris Cedex, France **/Comparative effects of apomorphine and naloxone in acutely defendent morphinized rats and mice./** Comparisons des effets de l'apomorphine et de la naloxone chez des rats et des souris en etat de dependance aigue a la morphine. Psychopharmacology (Berlin). 59(1):21-28, 1978.

The effect of acute morphine dependence on abstinence-like behavioral signs induced by apomorphine and naloxone was studied in Sprague-Dawley rats and two strains of mice. Acute morphinization decreased or increased the frequencies of various effects of apomorphine in rats, dependent on the particular sign and time schedule; these modifications were antagonized by naloxone. In mice, apomorphine produced infrequent jumping, which was enhanced considerably by morphine; this phenomenon was antagonized by naloxone. In morphinized mice, the jumping produced by apomorphine was antagonized by low doses of neuroleptics (haloperidol, chlorpromazine, pimozide, and benperidol), while jumping precipitated by naloxone was not antagonized even by high doses of haloperidol or chlorpromazine. Naloxone precipitated jumping was not antagonized by alpha-methyl-p-tyrosine. Results do not support the hypothesis that the abstinence-like signs produced by naloxone are dopaminergically mediated. 47 references. (Author abstract modified)

003380 Tyler, Corinnne B.; Schlemmer, R. Francis, Jr.; Narasimhachari, Nedathur; Davis, John M. Department of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **Behavioral changes induced by 2,5-dimethoxy 4-methyl-amphetamine (DOM, STP) in primate dyads.** Communications in Psychopharmacology. 2(4):337-342, 1978.

The behavioral effects of 2,5-dimethoxy 4-methylamphetamine (DOM), a hallucinogen, were studied in four adult Stumptail macaque female monkeys housed in pairs. Following a baseline observation period, 0.17mg/kg DOM was administered intramuscularly once daily for 5 days to one member of each pair. At the end of 1 week, there was a cross-over and the previously untreated monkeys received DOM treatment for 5 days. Upon acute administration, DOM induced decreases in the total initiated social activity, social grooming, self-grooming, and submissive gestures in treated monkeys. At the same time, DOM induced abnormal behavior including involuntary limb jerks, wet dog shakes, hypervigilance, and ptosis. During chronic administration, partial tolerance developed to DOM induced limb jerks, wet shakes, and ptosis but not to hypervigilance. It is suggested that this paradigm may provide a useful model system for the study of the psychopharmacology of DOM and other hallucinogens. 11 references. (Author abstract modified)

003381 Van Dongen, P. A. M.; Broekkamp, C. L. E.; Cools, A. R. Department of Pharmacology, University of Nijmegen, Geert Grooteplein N 21, Nijmegen, Netherlands **Atonia after carbachol microinjections near the locus coeruleus in cats.** Pharmacology Biochemistry and Behavior. 8(5):527-532, 1978.

The effect of microinjections of carbachol into the dorsolateral pontine tegmentum on the behavior of cats was investigated. Injections of small amounts of carbachol (50 and 500ng) into the pontine reticular formation induced muscular atonia in otherwise awake animals. The atonia was not due to cholinergic stimulation of the noradrenergic cells of the locus coeruleus or the dorsolateral pons, since the most effective sites were situated ventrally to the locus coeruleus and alpha-adrenergic and beta-adrenergic blocking agents did not affect the atonia. Results are discussed in view of the postualted role of the locus coeruleus in paradoxical sleep. 51 references. (Author abstract)

003382 Veith, Jane L.; Sandman, Curt A.; Walker, J. Michael; Coy, David H.; Kastin, Abba J. Department of Psychology, Ohio State University, 164 W. 19th Avenue, Columbus, OH 43210 **Systemic administration of endorphins selectively alters open field behavior of rats.** Physiology & Behavior. 20(5):539-542, 1978.

A single intraperitoneal injection of 100mg of alpha-endorphin, beta-endorphin, gamma-endorphin or their (D-Ala2) analogs was found to influence the behaviors of male albino Holtzman rats tested in the open field. Results show that beta-endorphin significantly increased grooming behavior whereas (D-Ala2)-alpha-endorphin appeared to enhance sexual arousal. Results also show that both gamma-endorphin and (D-Ala2)-gamma-endorphin affected separate measures indicative of heightened emotionality. It appears that systemic injections of these fragments of beta-lipotropin hormone are capable of modulating behaviors unrelated to analgesia. The selective effects of these peptides suggest that each may be coded to act upon receptor sites in a differential manner, resulting in separate and distinct patterns of behavioral alterations. 33 references. (Author abstract)

003383 Vetulani, Jerzy; Bednarczyk, Barbara; Reichenberg, Krystyna. Institute of Pharmacology, Polish Academy of Sciences, Smetna 12, 31-343 Krakow, Poland **Inhibition of "wet shakes" during morphine abstinence by an antagonist of opiate analgesia.** European Journal of Pharmacology (Amsterdam). 50(3):261-264, 1978.

An antagonist of morphine analgesia, N-cyclopropylmethylnorazidomorphine (CAM), inhibited the wet shakes appearing during spontaneous or nalorphine precipitated morphine abstinence. CAM inhibited the pinna reflex more strongly than did morphine and selectively antagonized quipazine induced head twitches; its inhibition of head twitches induced by 5-hydroxytryptophan or LSD seemed unspecific. Results suggest that the opiate receptors involved in the inhibition of some symptoms of morphine abstinence and of the pinna reflex differ from those involved in opiate analgesia. 13 references. (Author abstract)

003384 Vetulani, Jerzy; Melzacka, Miroslawa; Wiszniowska, Grazyna. Institute of Pharmacology, Polish Academy of Sciences, Smetna 12, 31-343 Krakow, Poland **Haloperidol depresses the accumulation of apomorphine in the striatum of the rat.** European Journal of Pharmacology (Amsterdam). 49(1):117-118, 1978.

To test whether the antagonism of haloperidal to apomorphine induced gnawing involved the action of the neuroleptic on apomorphine concentration in the striatum, rats were injected with haloperidol or saline, injected with apomorphine hydrochloride after 2 hours, and then decapitated. Apomorphine concentration in the striatum was assessed, and it was found that haloperidol pretreatment inhibited apomorphine accumulation in the striatum. The effect was dose dependent and was paralleled by reduction of gnawing behavior. It is concluded that the antagonism of haloperidol to apomorphine stereotypy is due to its inhibitory effect on accumulation of the dopamine receptor agonist. 5 references.

003385 Vijande, Manuel; Costales, Marina; Schiaffini, Omar; Marin, Bernardo. Department of Physiology, University of Oviedo, Oviedo, Spain **Agiotensin-induced drinking: sexual differences.** Pharmacology Biochemistry and Behavior. 8(6):753-755, 1978.

The dipsogenic effect of Angiotensin-2 (A-2), a putative thirst hormone, in relation to sexual variables was studied in Wistar rats. It was found that A-2 administered subcutaneously constitutes a stimulus that induces more drinking in females than in males. The adult females show maximum sensitivity to A-2 during proestrus. The males and females castrated at birth, and females androgenized at birth, drink similar volumes of water after A-2 injections. When castration is carried out in puberty or adulthood, there is a greater difference in the volume of water drunk after administration of A-2. In the intact animals, the females in their sexual cycle show maximum water injestion during the proestrus, statistically different from that of the estrus and the males. There is also a significant difference between the females at diestrus and the intact males. It is concluded that the pattern of stimulated intake is different in the two sexes, and appears to depend upon the development of the rats. 16 references. (Author abstract modified)

003386 Volkman, P. H.; Lorens, S. A.; Kindel, G. H.; Ginos, J. Z. Department of Pharmacology, Stritch School of Medicine, Loyola University, Maywood, IL 60153 **L-5-Hydroxytryptophan-induced myoclonus in guinea pigs: a model for the study of central serotonin-dopamine interactions.** Neuropharmacology (Oxford). 17(11):947-955, 1978.

Myoclonic responses produced in guinea-pigs by systemic administration of L-5-hydroxytryptophan (L-5-HTP) or of L-trypotophan plus a monoamine oxidase inhibitor, were recorded and analyzed quantitatively. Results indicate that L-5-HTP induced myoclonus involves 5-hydroxytryptamine (5-HT) neurons and receptors and is an all or none response due to a spillover phenomenon rather than to impulse release 5-HT. The myoclonus was antagonized by the 5-HT receptor blockers cyproheptadine and methergoline. Quipazine, an agent that releases 5-HT and inhibits its reuptake, production Injection of the 5-HT agonist, 5-methoxy-N, N-dimethyltryptamine, resulted in intense myoclonus and a behavioral syndrome characterized by writhing, turning, and hyperactivity. The dopamine (DA) receptor agonists apomorphine and N-n-propyl-N-n-butyl-beta (3,4-dihydroxyphenyl)-ethylamine hydrochloride antagonized the L-5-HTP induced myoclonus. The blockers DA receptor haloperidol and pimozide had no appreciable effect on L-5-HTP induced myoclonus, but antagonized the suppression of myoclonus by DA agonists. It is suggested that L-5-HTP induced myoclonus is a useful model for studying interactions between DA and 5-HT neuronal system, for screening new compounds for 5-HT and DA agonist and antagonist properties, and for screening potential anti-Parkinsonian agents. 36 references. (Author abstract modified)

003387 Wachtel, Helmut; Anden, Nils-Erik. Institut fur Neuropsychopharmakologie, Schering AG, Mullerstrasse 170-178, D-1000 Berlin 65, Germany **Motor activity of rats following intracerebral injections of drugs influencing GABA mechanisms.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 302(2):133-139, 1978.

Motor activity of rats was recorded following bilateral injections of gamma-aminobutyric acid (GABA) and the two GABA analogues gammahydroxybutyric acid (GHBA) and baclofen into the nucleus accumbens. GABA produced a short-lasting hypoactivity which was potentiated by the GABA transaminase inhibitor aminooxyacetic acid (AOAA). GHBA and baclofen produced more pronounced hypoactivity. Hypoactivity was followed by hyperactivity after GHBA, baclofen, and, to a lesser extent, AOAA plus GABA. Carnitine and betahydroxybutyric acid, which are structurally related to GABA and GHBA, were much less effective in inducing hypoactivity. Motor activity was stimulated by local treatment with the GABA receptor blocker picrotoxin but not by strychnine or pentylenetetrazole. GABA and GHBA inhibited apomorphine-induced activity in reserpine-treated rats, indicating that these compounds stimulate GABA receptors beyond the dopamine synapses. Motor activity was depressed by GHBA and GABA administered in the rostral and intermediate neostriatum and globus pallidus, and to a lesser extent, the caudal neostriatum. The stimulatory effect of GHBA or picrotoxin was less pronounced after local application to the globus pallidus or the neostriatum than to the nucleus accumbens. 35 references. (Author abstract modified)

003388 Waddington, John L.; Crow, Timothy J. Division of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow, HA1 3UJ, England **Methodological problems in the measurement of drug-induced rotational behaviour: continuous recording reveals time-course differences undetected by previous techniques.** Psychopharmacology (Berlin). 58(2):153-155, 1978.

Male Sprague-Dawley rats were lesioned unilaterally in the medial forebrain bundle with either the catecholamine neurotoxin 6-hydroxydopamine or the indoleamine neurotoxin 5,6-dihydroxytryptamine (5,6-DHT). Rotational responses in automated rotameters to apomorphine challenge were compared by four different techniques in current use and by assessment of complete rotation curves using both conventional statistical procedures and elementary computer derived elements of curvature. The rotational responses of the two groups, characterized neurochemically by identical depletions of striatal dopamine but with a greater depletion of striatal 5-hydroxytryptamine in 5,6-DHT lesioned animals, were indistinguishable using each of the four current techniques. Assessment of rotation curves revealed significant differences between the two groups, characterized by faster onset and offset of the rotational response in 5,6-DHT lesioned animals. Some current techniques may implicitly exclude the detection of such time course differences in rotational behavior. 12 references. (Author abstract modified)

003389 Wahlstrom, Goran. Department of Pharmacology, University of Umea, S-90187 Umea, Sweden **The effects of atropine on the tolerance and the convulsions seen after withdrawal from forced barbital drinking in the rat.** Psychopharmacology (Berlin). 59(2):123-128, 1978.

The effects of atropine on the tolerance and convulsions observed during the abstinence period following long-term barbital treatment were investigated in male Sprague-Dawley rats. Rats were forced to drink a barbital solution as their only drinking fluid for 33 weeks. During the subsequent withdrawal period, tolerance was recorded with a hexobarbital anesthesia threshold using an EEG criterion, and convulsions were recorded in jiggle cages. On days 3 and 28 of the abstinence period, intraperitoneal pretreatment with atropine (2, 4, and 8mg/kg) was given 1.5hours before threshold determinations. The barbital treatment induced a clear tolerance to hexobarbital, detectable through day 28 of abstinence. The largest dose of atropine reduced the hexobarbital threshold in tolerant and control rats at the time of maximum tolerance (day 3) and later during abstinence (day 28). Convulsions during abstinence were reduced for at least 8 hours after atropine treatment on day 3. Results suggest that cholinergic mechanisms are involved in the changes induced by chronic barbiturate treatment. 23 references. (Author abstract modified)

003390 Wauquier, A. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Internal stimulus conditioning to discriminative external stimuli.** Psychopharmacology (Berlin). 58(2):11, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, internal stimulus conditioning to discriminative external control was discussed. Internal cues produced by drugs or by intracranial self-stimulation can be brought under external stimulus control through classical conditioning procedures. The actions of some drugs known to disturb both external and internal stimulus control of behavior can be antagonized by antipsychotics. Experiments with these drugs may provide useful models of psychopathology, wherein the basic deficit is not a lack of behavioral reactivity but a dysfunction in feedback processes.

003391 Weiss, Bernard; Santelli, Shirley. Department of Radiation Biology and Biophysics, University of Rochester Medical Center, Rochester, NY 14642 **Dyskinesias evoled in monkeys by weekly administration of haloperidol.** Science. 200(4343):799-801, 1978.

The effect of haloperidol on movement was studied. In two cebus (Cebus albifrons) monkeys given weekly oral doses of 0.25mg of haloperiodol per kilogram, movement disorders appeared 1 to 8 hours after drug adminstration following the tenth weekly dose. These disorders included oral movements, peculiar postures, writhing, and stretching. Such reactions faded in intensity after the next two doses. Increasing the dose to 0.5mg/kg has elicited the disorders reliably after each weekly dose for almost 2 years. Similar reactions also developed in a squirrel monkey (Saimiri sciurea) treated weekly with haloperidol and in a third cebus monkey previously maintained for a year on a regimen of 0.25mg of haloperidol per kilogram on 5 days per week. These findings suggest an experimental model for determining the etiology of drug-induced movement disorders and an unrecognized clinical problem. 19 references. (Author abstract)

003392 Weissman, A. Pfizer Inc., Groton, CT 06340 **Generalization of the discriminative stimulus properties of delta9-tetrahydrocannabinol to cannabinoids with therapeutic potential.** Psychopharmacology (Berlin). 58(2):12, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the generalization of the discriminative stimulus properties of delta9-tetrahydrocannabinol (d9-THC) to cannabinoids with therapeutic potential was reported. Rats were trained to discriminate 3.2mg/kg intraperitoneal d9-THC from its vehicle solvent using a two lever fixed ratio 10 schedule. Drugs were administered intraperitoneally 1 hour prior to the 15 minute training or testing session. representative median effective doses for generalizing from d9-THC to test drug were: d9-THC, 0.74; nabilone, 0.22; racemic 9-nor-9beta-hydroxyhexahydrocannabinol (HHC), 0.56; cannabidiol, greater than 32; d8-THC, 2.33; cannbinol, 8.2; and 11-OH-d9-THC, 0.21mg/kg. In related experiments, nabilone was not discriminated as diazepam and HHC was not discriminated as morphine sulfate.

003393 Weissman, A. Pfizer Inc., Groton, CT 06340 **The discriminability of naloxone in rats depends on concomitant morphine treatment.** Psychopharmacology (Berlin). 58(2):12, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the discriminative stimulus properties of naloxone in rats narcotized with morphine was reported. One group of rats received saline (0.9%) or naloxone (3.2mg/kg) in the saline vehicle. In the second group, morphine sulfate (5mg/kg) was added to the saline vehicle or naloxone solution each day. Results indicate that naloxone is not robustly discriminated from saline unless morphine is administered concomitantly. Naloxone did not alter overall fixed ratio 10 response rates in Group I, but slightly elevated rates in Group II.

003394 White, Norman; Major, Robert. Department of Psychology, McGill University, 1205 McGregor Avenue, Montreal, Quebec, Canada H3A LBL **Effect of pimozide on the improvement in learning produced by self-stimulation and by water reinforcement.** Pharmacology Biochemistry and Behavior. 8(5):565-571, 1978.

The dopamine receptor blocker pimozide was administered to rats to determine the role of the dopaminergic nigro-neostriatal bundle in mediating the effects of brain stimulation reinforcement on memory. When rats self-stimulated immediately after the training trial of an appetitive task, their performance on a

retention test was improved the next day. This improvement was blocked by pretraining injections of pimozide. The drug also retarded learning on the same task when that occurred in the absence of a reinforcer. Findings indicate that pimozide can block certain effects of reinforcers in learning situations, but it is unlikely that the drug affects the formation of associations by acting on sensory or motor mechanisms. It is concluded that the dopaminergic nigro-neostriatal bundle mediates an effect of reinforcing events on behavior. 31 references. (Author abstract modified)

003395 Wilson, Marvin C.; Brenkert, Pam. Department of Pharmacology, School of Pharmacy, University of Missippi, University, MS 38677 **Effect of chronic cocaine treatment on limited access food consumption.** Communications in Psychopharmacology. 2(4):327-332, 1978.

Acute intraperitoneal pretreatment of male Sprague-Dawley rats with cocaine (10 and 20mg/kg) resulted in a significant decrease in 1 hour food ocnsumption, compared with vehicle controls. Cocaine (20mg/kg) was then administered intraperitoneally once daily for 30 days immediately after the food access period. On the day following the termination of this chronic dosing regimen, rats were again pretreated with the same dose as administered in the initial pretreatment session. The cocaine induced decrement in food consumption in this session was less than that in the initial session. These data indicate that sensitization did not develop to cocaine's effect on limited access food consumption. 10 references. (Author abstract mofified)

003396 Winter, J. C. Department of Pharmacology and Therapeutics, School of Medicine, State University of New York, Buffalo, NY 14214 **LSD-induced stimulus control: a comparison of Sch12,679, fenfluramine, p-methoxyamphetamine, and BL-3912.** Psychopharmacology (Berlin). 58(2):12, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a study of the generalization of stimulus control induced by lysergic acid diethylamine (LSD) was reported. Stimulus control was established with 0.1mg/kg LSD and saline in female albino rats using a two lever response choice task. Cross tests were conducted with Sch12,679 (N-methyl-7,8-dimethoxy-2,3,4,5-tetrahydro-3-benzazepine maleate), fenfluramine, p-methoxyamphetamine (PMA), and BL-3912, (alpha-methyl-2,5-dimethoxy-4-ethylphenylethylamine). With the exception of BL-3912, all of the cross tested drugs yielded intermediate results; responding was not fully appropriate for either training condition. In contrast, BL-3912 substituted completely for LSD. When animals were pretreated with BC-105, a serotonergic antagonist previously shown to be effective in blocking the stimulus effects of LSD and mescaline, the LSD-like effects of Sch12,679, fenfluramine, PMA, and BL-3912 were diminished.

003397 Wolfarth, S.; Dulska, E.; Golembiowska-Nikitin, K.; Vetulani, J. Institute of Pharmacology, Polish Academy of Sciences, PL-31-343 Krakow, 12 Smetna Str., Poland **A role of the polysynaptic system of substantia nigra in the cholinergic-dopaminergic equilibrium in the central nervous system.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 302(2):123-131, 1978.

Apomorphine and carbachol were injected stereotaxically, separately or in combination, into the substantia nigra (SN) of the rabbit to determine whether the dopaminergic and cholinergic systems of the SN are functionally antagonistic or agonistic. Apomorphine (2 micrograms) depressed locomotor activity and increased the relaxed EEG pattern, while carbachol (2 micrograms) increased locomotor activity, elevated the alert index, and produced episodes of epileptoidal discharges. Carbachol also produced sniffing, head turning, and rotations ipsilateral to the injection side. Pretreatment with apormorphine antagonized the epileptoidal discharges, sniffing, and rotation induced by carbachol. Apomorphine depressed the homovanillic acid (HVA) level in both striata, with the effect being highly significant only in the ipsilateral structure. HVA levels were weakly depressed after carbachol and were not affected by combined treatment with apomorphine and carbachol. Results indicate that the dopaminergic and cholingergic systems of the SN are mutually antagonistic. 54 references. (Author abstract modified)

003398 Woolverton, W. L.; Trost, R. C. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Cocaine as discriminative stimulus for responding maintained by food in squirrel monkeys.** Pharmacology Biochemistry and Behavior. 8(5):626-630, 1978.

The ability to discriminate low doses of cocaine from saline was examined in squirrel monkeys. Animals were trained in a choice procedure to discriminate a dose of 100microg/kg cocaine from saline. Following an injection of cocaine, responding on the right lever was reinforced with food, whereas following an injection of saline, responding on the left lever was reinforced. A high degree of stimulus control was established within 20 experimental sessions. The dose response function of cocaine on lever choice was then determined. When intermediate doses (10, 25, and 50microg/kg) were administered prior to test sessions, a dose dependent generalization decrement was observed. One monkey was able to discriminate as low as 25microg/kg cocaine from saline. 11 references. (Author abstract modified)

003399 Wuensch, Karl L.; Broome, Belinda; Means, Larry W.; Harris, Evans C., Jr. Dept. of Psychology, Miami University, Oxford, OH 45056 **Dorsomedial thalamic lesions and amphetamine: acquisition and retention of a visual pattern discrimination escape task.** Physiological Psychology. 6(3):288-293, 1978.

The performance of dorsal medial thalamus lesioned rats in a water filled maze, a task on which it was expected that the freezing often manifested by such animals in aversive situations would be eliminated as a possible explanation of deficit, was examined in two experiments. The lesioned animals showed both acquisition and retention deficits, but freezing-like behaviors were not eliminated as a possible interpretation. A third experiment effectively used amphetamine dosage to break up freezing-like responses, but no accompanying reduction in deficit was demonstrated. 18 references. (Author abstract)

003400 Yokel, Robert A.; Wise, Roy A. Department of Pharmacology, University of Cincinnati Medical Center, 231 Bethesda Avenue, Cincinnati, OH 45267 **Amphetamine-type reinforcement by dopaminergic agonists in the rat.** Psychopharmacology (Berlin). 58(3):289-296, 1978.

The hypothesis that amphetamine reinforcement is mediated by an effect on a dopaminergic system was tested in four experiments. In male Sprague-Dawley rats, intravenous self-administration of d-amphetamine (0.25mg/kg/injection) decreased in a dose related fashion after injections of the dopaminergic agonists apomorphine and piribedil. Clonidine, an alpha-noradrenergic agonist, did not have similar effects. Apomorphine and piribedil did not increase 14C-amphetamine levels in rat brains and did not retard disappearance of 14C-amphetamine. Rats responding for amphetamine continued to respond when apomorphine or piribedil were substituted. Rats experienced in amphetamine self-administration readily initiated and maintained responding for the dopaminergic agonists. The dopaminergic blocker ()-butaclamol disrupted responding for apomorphine and piribedil. Results indicate that actions in the dopaminergic

synapse account for the reinforcing properties of amphetamine. 34 references. (Author abstract modified)

003401 Young, Alice M.; Thompson, Travis. Department of Psychology, University of Minnesota, Minneapolis, MN 55455 **Effects of naloxone on schedule-controlled behavior in morphine-maintained tained pigeons.** Journal of Pharmacology and Experimental Therapeutics. 205(1):236-245, 1978.

The effects of repeated morphine administration and concurrent naloxone administration on the rate and pattern of keypecking maintained by a fixed-interval schedule of food presentation in the pigeon was investigated. The results show that the behavioral effects of the naloxone in pigeons receiving repeated morphine injections varied with the log dose of naloxone administered and correlated with the physiological abstinence sign of weight loss. Repeated daily administration of increasing doses of morphine, 9 to 90mg/kg/day, produced sustained decreases in overall rate of keypecking across all doses over a period of 24 to 25 weeks. Naloxone altered overall rate of keypecking in a dose related manner. The findings show in the first series of naloxone challenges, low doses (0.01 and 0.03mg/kg) slightly increased overall rate, higher doses decreased overall rate, with complete response suppression occurring at 0.30 to 1.0mg/kg. Naloxone decreased overall rate at lower doses in the second administration series than in the first. Increases in total session pause time paralleled the naloxone produced decreases in overall rate. Naloxone generally altered running rate of keypecking in an all or none fashion. 28 references. (Author abstract modified)

003402 Young, John K.; Nance, Dwight M.; Gorski, Roger A. Department of Anatomy and Brain Research Institute, University of California, Los Angeles, CA 90024 **Dietary effects upon food and water intake and responsiveness to estrogen, 2-deoxyglucose and glucose in female rats.** Physiology & Behavior. 21(3):395-403, 1978.

The effects of ovariectomy, estradiol benzoate (EB), 2-deoxyglucose (2-DG), and ad lib glucose solutions on feeding were investigated in female Sprague-Dawley rats maintained on chow, high dextrose, or high fat diets. Rats on the high fat diet responded significantly more to EB, 2-DG, and ad lib glucose than did rats on the chow or high dextrose diets; increased responses to EB were not explainable on the basis of increased bodyweight. Rats on the high dextrose diet chronically maintained a lowered calorie intake, water intake, and body weight, in spite of the high palatability of the dextrose diet. Responses of dextrose fed animals to EB showed a high correlation with bodyweight, suggesting an augmented influence of a weight related signal on feeding regulation. A possible relationship between carbohydrate metabolism and responsiveness to EB is discussed. 36 references. (Author abstract)

003403 Young, Randall D.; Thorn, Beverly E.; Levitt, Robert A.; Weyant, Maxine J. Department of Psychology, Southern Illinois University, Carbondale, IL 62901 **Use of the flinch-jump technique to study narcotic analgesia in the rat.** Physiological Psychology. 6(2):226-228, 1978.

The flinch/jump technique was adapted to allow single-session, within subject evaluation of narcotic analgesia and its blockade by a narcotic antagonist in Long-Evans rats. Morphine (2.4, 5.0, and 10.0mg/kg) produced dose related analgesia, while injection of saline or the narcotic antagonist naloxone failed to alter jump thresholds. Injection of 0.1or 1.0mg/kg naloxone systematically reversed the analgesia produced by 10mg/kg morphine. 12 references. (Author abstract modified)

003404 Zackova, P.; Vlkova, A.; Kvetina, J.; Zamazalova, I. Charles University, Dept. of Pharmacology and Toxicology, Heyrovskeho 1203, Hradec Kralove, Czechoslovakia **Comparison of the effect of some benzodiazepines with the "staircase" method.** Activitas Nervosa Superior (Praha). 29(1):75-76, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, comparison of the effect of some benzodiazepines on rats via the staircase method is described. The staircase method allowed for observation of the effects of a drug on various components of exploratory and emotional behavior. A comparison of diazepam, nitrazepam, oxazepam, medazepam, and chlordiazepoxide showed that the most intensive suppression of walking was induced by diazepam. All benzodiazepines administered decreased rearing.

05 TOXICOLOGY AND SIDE EFFECTS

003405 Akera, Tai; Ku, David D.; Brody, Theodore M.; Manian, Albert A. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Inotropic action of hydroxylated chlorpromazine metabolites and related compounds.** Biochemical Pharmacology (Oxford). 27(6):995-998, 1978.

Effects of several hydroxylated chlorpromazine metabolites and related compounds on cardiac contractile force were studied in electrically stimulated left atrial preparations of guinea pig hearts. Both 7,8-dihydroxychlorpromazine and 7,8-dioxochlorpromazine produced marked positive inotropic effects in mcM concentrations, while 7,8-dihydroxyperphenazine, 7-hydroxychlorpromazine, and 2-hydroxydesmethylimipramine had weak inotropic action. Other compounds, such as chlorpromazine, 8-hydroxychlorpromazine, 2-hydroxypromazine, 3-hydroxypromazine, and 2-hydroxyimipramine, failed to significantly alter cardiac contractile force. The positive inotropic effects of 7,8-dihydroxychlorpromazine and 7,8-dioxochlorpromazine were markedly reduced by pretreatment with propranolol, indicating the involvement of beta-adrenergic mechanisms in the inotropic action of these agents. 20 references. (Author abstract modified)

003406 Biziere, K.; Coyle, J. T. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Effects of kainic acid on ion distribution and ATP levels of striatal slices incubated in vitro.** Journal of Neurochemistry (Oxford). 31(2):513-520, 1978.

To determine the mechanism of neurotoxicity of kainic acid, striatal slices (350mcm) from male Sprague-Dawley rats were incubated in oxygenated Krebs buffer, and alterations in the uptake and retention of 22Na, 86Rb (as a measure of K), and 3H2O and the levels of adenosine triphosphate (ATP) were determined. Although 10mM kainate significantly depressed striatal K and ATP, lower concentration of kainate (5mM-0.1microM) elevated striatal uptake of Na but did not markedly affect H2O, K, or ATP. Kainate (10mM-1mcM) did not show additivity with 10mM glutamate with respect to Na permeability but did significantly potentiate glutamate's ATP depleting effects. Injection of 10nM of kainate into the striatum in vivo caused a reduction in striatal ATP one hour afterward, which was comparable to that occurring in vitro with 10mM kainate alone or with lower concentrations of kainate in combination with 10mM glutamate. Results suggest that kainate alone is directly neurotoxic at 10mM or neurotoxic at lower concentrations in combination with the high intrasynaptic levels of glutamate on neurons receiving glutaminergic innervation. Additional tests with L-glutamate, N-methyl aspartate, veratridine, and ouabain confirmed the validity of the in vitro method used. 37 references. (Author abstract modified)

003407 Cann, Frank James. Loyola University of Chicago **Pharmacological, behavioral and neurochemical assessment of the**

selectivity of the destruction of central serotonergic and catecholamingergic mechanisms by 6-hydroxydopamine and 5,6-dihydroxytryptamine in the mouse. (Ph.D. dissertation). Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 787063, HC$15. MF$7.50. 200 p. 1978.

The effects of two neurotoxic compounds, 5,6-dihydroxytryptamine (5,6-OHT) and 6-hydroxydopamine (6-OHDA) were compared for their selectivity of action in mice when administered by the intracerebroventricular route. Selectivity was assessed by measuring the brain contents of four neurotransmitters: dopamine, norepinephrine, serotonin and acetylcholine. Data suggest that central postsynaptic receptor supersensitivity may be specific in nature, which is in marked contrast to its nonspecific nature in the peripheral nervous system. The nature of central postsynaptic receptor sensitivity is discussed in detail. It is noted that, if the postsynaptic receptor changes are specific in nature, as is suggested by the data, then they may be exploited with neuropsychodiagnostic agents to help elucidate the nature of dysfunction and subsequent treatment in neuropsychopathological states, whether these be neurological, emotive, or cognitive in nature. (Journal abstract modified)

003408 Dewar, A. J.; Yates, Celia M.; Barron, Gillian; Gordon, A.; Wilson, Helen; Baker, Janet. Shell Toxicology Laboratory (Tunstall), Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England **The effects of chronic chlorpromazine administration on the albino rat retina.** Toxicology and Applied Pharmacology. 43(3):501-506, 1978.

Chlorpromazine (CPZ, 2 to 35mg/kg/day) was administered orally to male albino Wistar rats for 13 months to determine its effect on the retina. Even in doses toxic enough to produce a 32% reduction in bodyweight, CPZ had no observable effect on the retina. CPZ inhibited retinal cyclic adenosine monophosphate phosphodiesterase activity in vitro but did not alter enzyme activity in vivo. This lack of effect in vivo was probably related to the very low CPZ serum concentrations which were less than 1% of the concentration required to inhibit the enzyme activity in vitro. 16 references.

003409 Doak, R. L.; Holman, R. B.; Elliott, G. R.; Seagraves, E.; Barchas, J. D. Division of Laboratory Animal Medicine, Stanford University School of Medicine, Stanford, CA 94305 **Toxicity of 5-hydroxytryptoline in rats.** Toxicology and Applied Pharmacology. 45(3):729-737, 1978.

The toxicity of 5-hydroxytryptoline (5-HTLN), a cyclic analogue of 5-hydroxytryptamine, was studied in male Sprague-Dawley rats receiving daily intraperitoneal injections of saline for 7 days or of 100mg/kg 5-HTLN for 1, 7, or 10 days prior to sacrifice. At this dose, 5-HTLN produced marked nephrotoxicity, with serum elevations of blood urea nitrogen, creatinine, and inorganic phosphate in some animals. Histological examination of the kidneys revealed a pattern of acute tubular degeneration and necrosis and glomerular membrane damage, along with evidence of tubular regeneration in some animals. There was also mild hepatocellular degeneration in some animals, without consistent elevations in related serum enzymes. No abnormalities were found in other organ tissues, including brain, adrenals, pancreas, heart, lung, and gastrointestinal tract. Terminal hematological data were normal. 20 references. (Author abstract)

003410 James, Robert C.; Franklin, Michael R. Division of Clinical Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232 **The triphasic amphetamine lethal dose curve in mice and its possible relationship to drug metabolism.** Toxicology and Applied Pharmacology. 44(1):63-73, 1978.

The possible relationship between metabolism and the triphasic lethal dose curve of d-amphetamine was investigated in ICR mice. Inhibition of hepatic oxidative metabolism with diethylaminoethyl 2,3-diphenylvalerate hydrochloride, 2,4-dichloro-6-phenylphenoxyethyldiethylamine hydrobromide, or piperonyl butoxide abolished the triphasic response in mortality that is usually obtained for the lethal dose curve of d-amphetamine in mice. CNS properties of these agents were not responsible for this change. Although inhibitory amphetamine metabolic intermediate (MI) complexes were formed in mouse microsomes in vitro, only very small amounts of amphetamine MI complexes were found in vivo. It is concluded that amphetamine MI complexes do not affect amphetamine metabolism and are not involved in the mechanisms whereby changes in metabolism affect mortality. 27references. (Author abstract)

003411 Jori, A.; Rutczynski, M. Istituto di Ricerche Farmacologiche 'Mario Negri' via Eritrea, 62, I-20157 Milan, Italy **A genetic analysis of the hyperthermic response to d-amphetamine in two inbred strains of mice.** Psychopharmacology (Berlin). 59(2):199-203, 1978.

A genetic analysis of amphetamine-induced hyperthermia was conducted in inbred mice of the strains Balb/c and C3H and in their F1F2 and backcross generations. The results of biometric analysis indicate that the effect of amphetamine on body temperature is genetically determined. The mode of inheritance is characterized by partial dominance (Balb/c over C3H strain). However, a possible maternal effect of C3H can overcome the dominant effect in male progenies and inhibit the amphetamine hyperthermic effect. 17 references. (Author abstract)

003412 LeLorier, J. Department de Pharmacologie, Faculte de Medecine, Universite de Montreal, Montreal, Quebec, Canada H3C 3J7 **Lidocaine and pentobarbital: a potentially lethal drug-drug interaction.** Toxicology and Applied Pharmacology. 44(3):657-659, 1978.

To explore the possibility of an interaction between lidocaine and pentobarbital, six unanesthetized dogs were given lidocaine infusions according to a schedule that produced therapeutic lidocaine plasma concentrations at a steady state after 30 minutes. Six control dogs received equivolumetric infusions of normal saline. Ninety minutes after the beginning of the infusions, dogs in both groups were given 30mg/kg pentobarbital, administered intravenously over a period of 1 minute. All lidocain treated dogs developed apnea and four died. None of the saline infused dogs died, and only one developed apnea. It is concluded that simultaneously administered lidocaine and pentobarbital are toxic, probably as a result of additive depressant effects on the respiratory center. The possibility of this interaction should be taken into consideration whenever these two drugs are prescribed simultaneously. 7 references. (Author abstract)

003413 Marini, James L.; Williams, S. P.; Sheard, M. H. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06508 **Repeated sustained-release lithium carbonate administration to cats.** Toxicology and Applied Pharmacology. 43(3):559-567, 1978.

Lithium carbonate (0.6to 1.1meq/kg/day) was administered to 10 cats for up to 18 consecutive days, in single daily oral doses of a sustained release preparation. The animals tolerated 0.6meq/kg/day well, with little or no weight loss or other signs of toxicity; renal lithium clearance was efficient and 24 hour serum lithium concentrations were stable. Although some cats tolerated higher doses (0.8to 0.9meq/kg/day) well for 4 to 5 days, doses greater than 0.85meq/kg/day generally produced pronounced weight loss, often impaired renal lithium clearance.

and gave high (greater than 1meq/liter) 24 hour serum lithium concentrations. 7 references. (Author abstract modified)

003414 Nielsen-Kudsk, F.; Pedersen, A. Kirstein. Institute of Pharmacology, University of Aarhus, DK-8000 Aarhus C, Denmark **Myocardial pharmacokinetics of lithium in vitro.** Acta Pharmacologica et Toxicologica (Copenhagen). 42(4):303-310, 1978.

The myocardial pharmacokinetics of ionized lithium were investigated in the isolated, intact rabbit hearts, which were retrogradely perfused with a modified Krebbs-Henseleit solution containing 5mM lithium. The rates of accumulation and disposition of lithium fit biexponential functions, as an expression of the myocardium behaving as a two compartment system obeying first order, linear kinetics with respect to ionized lithium. A pronounced decrease of the uncomposite elimination rate constants k10 and especially k21 was observed after continuous lithium perfusion for about 30 minutes. During this perfusion period at steady state, an absolute increase of myocardial lithium accumulation occurred. A possible correlation of these findings with the cardiac effects of lithium is discussed. 21 references. (Author abstract modified)

003415 Nielsen-Kudsk, F.; Pedersen, A. Kirstein. Institute of Pharmacology, University of Aarhus, DK-8000 Aarhus C, Denmark **Myocardial effects of lithium in vitro.** Acta Pharmacologica et Toxicologica (Copenhagen). 42(2):311-316, 1978.

The myocardial effects of ionic lithium were investigated in isolated spontaneously beating rabbit hearts, which were retrogradely perfused with a modified Krebbs-Henseleit solution containing 1, 5, or 10mM lithium. The lowest lithium concentration caused no measurable changes in heartrate, amplitude and rate of contraction, coronary flow, myocardial oxygen consumption, or electrocardiogram. A concentration of 5mM lithium produced an increase in amplitude and rate of contraction of about 22%, without a concomitant increase in oxygen consumption. A delayed increase in oxygen consumption of about 21% accompanied by a significant decrease in oxygen consumption occurred later in the experiment, probably as an expression of a decrease in myocardial efficiency. The highest lithium concentration produced similar effects. In rabbit papillary muscles lithium had a positive inotropic effect on myocardial contractility that could not be abolished by adrenergic beta-receptor blockade. Possible effects of lithium on cellular calcium metabolism are discussed. 22 references. (Author abstract modified)

003416 no author. no address **Common drugs seen as potential carcinogens.** Medical World News. 19(16):56, 1978.

The announcement to the American Chemical Society by Dr. William Lijinsky that research animals fed nitrites and chlordiazepoxide (Librium) or oxytetracycline (Terramycin) developed significantly more tumors than those fed nitrites alone, is reported. This finding, together with the recent report that diazepam (Valium) harms chick embryo muscle cells in vitro have caused concern over the widespread use of these psychotropic medications by humans. Research results suggests that when a dietary amine meets an ingested nitrite in the acid environment of the stomach, the result is a nitrosamine that may be carcinogenic

003417 Refsum, Helge; Passwal, Masjedi; Olsson, Sven-Olle. Institute of Medical Biology, University of Tromso, N-9000 Tromso, Norway **Comparison of the electrophysiological effects of two neuroleptics, melperone and thioridazine, on isolated rat atria.** European Journal of Pharmacology (Amsterdam). 49(3):285-293, 1978.

The effects of two neuroleptics, melperone (a butyrophenone) and thioridazine (a phenothiazine), on the electrical and mechanical activity of isolated rat atria were investigated. Melperone prolonged the effective refractory period without significantly altering the threshold for electrical stimulation (excitability). Thioridazine caused a similar prolongation of the effective refractory period, but also significantly decreased excitability. In contrast to melperone, thioridazine had a negative ionotropic effect. The spontaneous pacemaker activity was depressed and the sinus node recovery time increased to a greater extent after melperone than after thioridazine. Findings suggest that melperone may be a type III antiarrhythmic, while thioridazine may be a type I agent. Results also indicate that melperone may act as an antiarrhythmic agent by depressing automaticity. 44 references. (Author abstract modified)

003418 Seil, Fredrick J.; Woodward, William R.; Blank, Nathan K.; Leiman, Arnold L. Department of Neurology, University of Oregon Health Sciences Center, Portland, OR **Evidence against chronic depolarization as a mechanism of kainic acid toxicity in mouse cerebellar cultures.** Brain Research (Amsterdam). 159(2):431-435, 1978.

The mechanism of kainic acid toxicity was examined in mouse cerebellar cultures. The cultures were incubated in nutrient medium supplemented with L-glutamic acid or D-glutamic acid or with combinations of kainic acid and gamma-aminobutyric acid (GABA). The depolarizing amino acids L-glutamic acid and D-glutamic acid failed to simulate kainic acid toxic effects in the cerebellar cultures. L-glutamic acid and GABA both failed to competitively inhibit the toxic effects of kainic acid. Results suggest that the neurotoxic effects of kainic acid are not mediated exclusively by action on putative glutamic acid receptors and that kainic acid does not produce its toxic effects by lethal neuroexcitation. 8 references.

003419 Sethi, N.; Sethi, B. B. Central Drug Research Institute, Lucknow, India **Effects of some of the neuroleptics on the reproductive organs of rats.** Indian Journal of Psychiatry (Lucknow). 20(1):37-42, 1978.

The effects of tranquilizers and antidepressant drugs on the reproductive organs and pregnancy rates of 140 Charles Foster rats were studied. Butyrophenones, phenothiazine derivatives, and reserpine were found to have similar actions in lowering fertility, while MAO inhibitors did not affect fertility rate. These findings are in harmony with the widely discussed neuroendocrine regulation concept according to which hypothalmo/hypophyseal complex gets disturbed and is followed by disturbances in the function of different organs. While reduction in the size of reproductive organs suggest a lower level of gonadotrophin, a higher level of prolactin explains the activity of mammary glands. 10 references.

003420 Toews, Arrel D.; Kolber, Alan; Hayward, Jean; Krigman, Martin R.; Morell, Pierre. Department of Biochemistry, University of North Carolina, Chapel Hill, NC 27514 **Experimental lead encephalopathy in the suckling rat: concentration of lead in cellular fractions enriched in brain capillaries.** Brain Research (Amsterdam). 147(1):131-138, 1978.

Five-day-old Long-Evans rats subjected to 2 day lead (Pb) exposure by gastric gavage of aqueous Pb acetate at the highest nonlethal dosage (1mg Pb/g body weight/day) developed a hemorrhagic encephalopathy. Capillaries and microvessels isolated from brains of these rats showed abnormal morphology consisting of an increased number of irregularly dispersed endothelial nuclei and swollen, vacuolated endothelial cells. Pb was concentrated in isolated brain capillary/microvessel fractions, as demonstrated by both atomic absorption and 210Pb microtracer methods. When Pb exposure was continued for 20 days at the maximal dosage regime compatible with a 60% survival rate,

the rats recovered from the initial encephalopathy; capillaries and microvessels isolated from brains of these rats appeared morphologically normal. This recovery occurred despite continued high levels of Pb in the blood and in the isolated capillary/microvessel fractions, suggesting that capillary endothelial cells are able to adapt to the presence of large amounts of lead as they mature. 21 references. (Author abstract modified)

003421 Woolverton, W. L.; Schuster, C. R. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **The effects of daily cocaine administration on cocaine-induced mortality.** Research Communications in Psychology, Psychiatry and Behavior. 3(3):257-265, 1978.

Change in sensitivity to the lethal effects of cocaine as a result of daily cocaine administration are studied in 100 male albino Sprague-Dawley derived rats. Dosage mortality determinations for cocaine were made in rats that had received 45 daily injections of either 30mg cocaine per kg of body weight, or saline. Lethal dosages were calculated using the Bliss method for determining a dosage mortality curve from small numbers. Daily administration of cocaine was not found to alter the lethal effects of cocaine. 13 references. (Author abstract modified)

06 METHODS DEVELOPMENT

003422 Algate, D. R.; Leach, G. D. H. Wyeth Institute of Medical Research, Huntercombe Lane South, Taplow, England **Dopamine-beta-hydroxylase release following acute selective sympathetic nerve stimulation of the heart, spleen and mesentery.** Journal of Pharmacy and Pharmacology (London). 30(3):162-166, 1978.

The relationship between the serum concentration of dopamine-beta-hydroxylase (DBH) and the state of sympathetic nerves was explored to test the hypothesis that changes in the circulation plasma DBH concentration do not accurately reflect changes in the sympathetic nerve system. Following selective sympathetic nerve stimulation of pithed female rats, an increase in the concentration of DBH was detected in the blood perfusates of the heart, spleen, and mesentery. The concentration of DBH released by each organ correlated with the stimulation frequency. The results indicate that the concentration of DBH in the plasma is related to the degree of sympathetic tone. It is suggested that similar methods could be used in nonspinalized animals to provide an index of sympathetic nervous tone; measurement of DBH concentrations in organ perfusates could be a useful preparation for the study of drugs on the sympathetic nervous system. 14 references. (Author abstract modified)

003423 Berger, Brigitte; Glowinski, Jacques. INSERM U 134, Laboratoire de Neuropathologie Charles Foix, Hopital Salpetriere, F-75634 Paris Cedex 13, France **Dopamine uptake in serotoninergic terminals in vitro: a valuable tool for the histochemical differentiation of catecholaminergic and serotoninergic terminals in rat cerebral structures.** Brain Research (Amsterdam). 147(1):29-45, 1978.

An in vitro method was developed to separately visualize dopaminergic, noradrenergic, and serotoninergic terminals in the cerebral, hippocampal, and cerebellar cortices of the rat, using glyoxylic histochemical fluorescence. Animals were pretreated with alpha-methyl-p-tyrosine to deplete catecholamine stores. Thin vibratome sections were made and incubated in the presence of various exogenous amines and inhibitors of the catecholaminergic and serotoninergic transport systems. The validity of the combined pharmacological and histochemical approach was also tested in animals in which the cortical dopaminergic, noradrenergic, or serotoninergic innervations were destroyed by chemical or electrolytic lesions. Under the experimental conditions used, norepinephrine and alpha-methylnorepinephrine were taken up only in noradrenergic and dopaminergic terminals. A separate visualization of the two systems was obtained by using specific uptake inhibitors. Dopamine was taken up not only in catecholaminergic terminals, but also in serotoninergic terminals. The uptake of dopamine in serotoninergic fibers was inhibited by a specific inhibitor of serotoninergic transport or by the presence of serotonin in the incubating medium. 43 references. (Author abstract)

003424 Fuentes, Victor O.; Hunt, William B.; Crossland, James. Department of Pharmacology, Faculty of Veterinary Medicine UNAM, Mexico **The production of morphine tolerance and physical dependence by the oral route in the rat.** Psychopharmacology (Berlin). 59(1):65-69, 1978.

A newly developed method for the chronic administration of morphine to rats by the oral route is described. Morphine chloride is dissolved in a 45% sucrose syrup and given orally for 4 weeks. The initial concentration of morphine in the syrup is 1mg/ml and is increased weekly up to 4mg/ml. Using this procedure, animals can be rendered physically dependent on morphine, as evidenced by abstinence symptoms when the drug is withdrawn. The advantage of this oral method over the more traditional injection method for producing morphine tolerance and physical dependence are discussed. 33 references. (Author abstract modified)

003425 Gulliver, Peter A.; Tipton, Keith F. Department of Biochemistry, University of Cambridge, Tennis Court Road, Cambridge, CB2 1QW, England **Direct extraction radioassay for catechol-O-methyl-transferase activity.** Biochemical Pharmacology (Oxford). 27(5):773-775, 1978.

An improved radiochemical assay for catechol-O-methyl transferase that is particularly suitable for use with large numbers of samples is described. 3,4-Dihydroxyphenylacetic acid is converted to radioactively labeled homovanillic acid in the presence of s-adenosyl-L-(methyl-3H)methionine. This product is extracted into an organic solvent/scintillant mixture. Scintillation counting is performed without further manipulation. 14 references. (Author abstract)

003426 Jenden, Donald J.; Roch, Margareth; Fainman, Francine. Department of Pharmacology, University of California, Los Angeles, CA 90024 **Estimation of deanol and choline by gas chromatography mass spectrometry.** Life Sciences. 23(4):291-300, 1978.

Analytical methods are described which permit the measurement of both deanol and choline in the same sample by gas chromatography mass spectrometry when either compound may be present in large excess (100:1). Deuterium labeling is employed for internal standards, to distinguish endogenous from tracer variants and to distinguish deanol in the sample from deanol formed by derivatization of choline. The limit of detection of both compounds is about 50pmol. 42 references. (Author abstract)

003427 Kubacki, Andrzej. Mental Health Clinic, c/o Chaleur General Hospital, Bathurst, New Brunswick, Canada **Mandibulogram as a measure of stereotyped behavior in the rat.** Psychopharmacology (Berlin). 59(2):209-210, 1978.

A bioelectric device for the continuous and quantifiable monitoring of movements of the mandible in rats is described. The device can be used in experimental psychopharmacology to monitor the effects of neuroleptics and antidepressants on oral stereotypies induced by CNS stimulants. The combination of the mandibulogram and the electromyogram affords innumerable applications in the detailed analysis of gnawing behavior, such as the differentiation of spontaneous and drug-induced move-

ments, the effects of CNS stimulants, and recognition of artifacts. 5 references. (Author abstract modified)

003428 Lal, H. Department of Pharmacology, University of Rhode Island, Kingston, RI 02881 **Interoceptive discriminative stimuli as tools in drug development.** Psychopharmacology (Berlin). 58(2):7, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, the use of interoceptive discriminative stimuli (IDS) as tools in drug development was discussed. IDS are the quantifiable subjective experiences that result from physiological changes occurring within the body. Through comparative studies with the IDS of known drugs, new chemicals can be classified as hypnotics, anxiolytics, antiepileptics psychomotor simulants, euphoriants, antihallucinatory agents, antiemetics, and narcotic agonists or antagonists. IDS are potentially useful in behavioral toxicology, in studies of the sites and mechanisms of drug action, and in identifying different actions of the same drug. IDS are now being explored as animal models of addiction, headache, visceral pain, inflammation, central hypertension, epilepsy, dysphoria, and euphoria. (Author abstract modified)

003429 Linnoila, M.; Dorrity, F. Department of Psychiatry, Duke University Medical Center, Durham, NC 27710 **Measurement of plasma and erythrocyte chlorpromazine and N-monodesmethylchlorpromazine levels by gas chromatography with a nitrogen sensitive detector.** Acta Pharmacologica et Toxicologica (Copenhagen). 42(4):264-270, 1978.

A new gas chromatographic method, employing a nitrogen-phorphorus sensitive detector, for the measurement of chlorpromazine (CPZ) and N-monodesmethylchlorpromazine (DMCPZ) is described. The application of the method to the measurement of the drugs in clinical plasma and erythrocyte samples is demonstrated. It was found that the CPZ concentration in the erythrocytes is positively and linearly correlated with the drug level in plasma. However, a fourfold interindividual variation in the erythrocyte/plasma concentration ratios was evident. The concentration of DMCPZ in the erythrocytes was found to be up to 27% of that of the parent compound. CPZ was unstable in plasma but stable in erythrocytes during a week's storage in the dark at 20 degrees. Possible clinical implications of these findings are discussed. 19 references. (Author abstract modified)

003430 Mann, Stephen P. Agricultural Research Council, Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **An improved assay of tyrosine hydroxylase using sodium activation.** Journal of Neurochemistry (Oxford). 31(3):747-749, 1978.

An improved assay of tyrosine hydroxylase using sodium activation is described. Acetone powders prepared from guinea-pig caudate nucleus were incubated with increasing mounts of sodium chloride (NaCl) and potassium chloride (KCL). The enzyme activity increased with the concentration of salt; maximal activity was obtained with 400mM NaCl or KCl. Centrifuged homogenates were not activated by either salt. NaCl and KCl increased the maximum velocity of the enzymes in acetone powders without significantly altering the Michaelis-Menten constant values by a direct action on the enzyme. The TH values obtained for the caudate (2.3ol/g 4 hour) and whole brain (o.mol/g 1 hour) are considerably higher than those reported by other researchers. 8 references.

003431 Martin, Ian L.; Baker, Glen B.; Fleetwood-Walker, Susan M. MRC Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **Modification of the radioenzymatic assay for the catecholamines.** Biochemical Pharmacology (Oxford). 27(11):1519-1520, 1978.

The catecholamine radioenzymatic assay using catechol-O-methyl transferase with radioactively labeled S-adenosyl methionine (SAM) was modified to permit the separation and purification of the catecholamines by thin layer chromatography. The procedure involves the enzymatic transfer of the radioactively labeled methyl group of SAM to the phenolic function at the 3 position of the catecholamine, subsequent purification of the radioactively labeled product, and quantification by liquid scintillation counting. The method is sensitive, reproducible, and rapid. 5 references. (Author abstract modified)

003432 McGovern, A. J.; Makanjuola, R.; Arbuthnott, G. W.; Loudon, J. B.; Glen, A. I. M. MRC Brain Metabolism Unit, University Department of Pharmacology, 1 George Square, Edinburgh, EH8 9JZ, Scotland **Lithium neurotoxicity. I. The concentration of lithium in dopaminergic systems of rat brain determined by flameless atomic absorption spectrophotometry.** Acta Pharmacologica et Toxicologica (Copenhagen). 42(4):259-263, 1978.

A method was developed for accurately measuring lithium concentrations in 10-100 amounts in less than 10-100mg fresh weight of brain tissue, using flameless atomic absorption spectrophotometry. In experiments where rats were fed lithium over a period of 3 weeks, no direct association of lithium with an area predominantly served by dopamine receptors could be confirmed by this method. Flameless atomic absorption spectrophotometry offers a method for analysis of lithium in discrete areas of brain where the amount of tissue available prevents analysis by conventional methods. 11 references. (Author abstract modified)

003433 Meibach, Richard C.; Brown, Lucy; Brooks, Fran H. Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, NY 10461 **Histofluorescence of kainic acid-induced striatal lesions.** Brain Research (Amsterdam). 148(1):219-223, 1978.

Histochemical techniques were used in an attempt to obtain anatomical evidence to support the suggestion that kainic acid acts as a specific perikarya neurotoxin, without involvement of adjacent fibers and axon terminals. Following injection of 2.5mcg kainic acid in the central portion of the rat caudoputamen, extensive depletion of dopamine in the striatum was observed. Due to the limits of the histofluorescence technique, it cannot be definitely concluded that this dopamine loss was due to degeneration of nigrostriatal neurons. However, the failure of anatomical methods to confirm previous biochemical observations of the restricted effect of kainic acid on cell bodies suggests that widespread use of kainic acid as a specific perikarya neurotoxin is not warranted at this time. 9 references.

003434 Overton, D. A. Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA **Optimal training compartment design, schedule of reinforcement and shaping procedures to establish 2-bar operant drug discriminations.** Psychopharmacology (Berlin). 58(2):9, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, a comparative study of various two bar drug discrimination methods was reported. Training compartment design, reinforcement schedules, and shaping procedures were varied to determine which would produce the most rapid acquisition and highest asymptotic accuracy. Training with an interlocking fixed-interval/ fixed-ratio schedule, using appropriate drug conditions throughout initial shaping, allowed an average accuracy of 95% to be achieved within 10 days of training. Good discrimination was obtained in the standard training compartment with two bars side by side on one wall with the reinforcement magazine be-

tween them; discrimination accuracy was not improved when a unique sensory environment surrounded each bar and wasimparied when placed on opposite walls of the box.

003435 Rosenfeld, J. Peter; Broton, James G.; Clavier, Ronald M. Department of Psychology, Northwestern University, Evanston-Chicago, IL 60201 **A reliable, facial nociception device for unrestrained, awake animals: effects of morphine and trigeminal complex lesions.** Physiology & Behavior. 21(2):287-290, 1978.

A new technique for quantifying orofacial pain in unrestrained, freely moving rats is described. The key dependent variable is latency to a face rubbing response executed with any paw. The response is elicited by heating a tiny resistor in contact with facial skin. The latency variability is significantly less than that of hotplate/paw lick and other measures. The measure has been used to precisely index effects of morphine, trigeminal complex lesions, and heat rate manipulations. It is noted that the technique should be useful in pain and analgesia research. Use of the face as site of nociceptive stimulation also has special relevance for studies of nociceptive aspects of the trigeminal system it is suggested. 8 reference. (Author abstract)

003436 Smith, Stanley G.; Werner, Toreen E.; Harland, Ernest C.; Davis, W. Marvin. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Esophageal cannulation for intragastric delivery of fluids to unrestrained dogs.** Physiology & Behavior. 21(4):659-661, 1978.

A method of esophageal cannulation for intragastric administration of solutions or suspensions to the dog is described. The method permits single or repeated oral dosing without stress to the dog; postoperative recovery time is short and no vomiting occurs. The method allows study of drug self-administration behavior with compounds not readily examined by oral ingestion because of taste or by parenteral routes because of insolubility or toxicity. 7 references. (Author abstract)

003437 Smith, Stanley George. University of Mississippi **The effects of intragastric morphine self-administration in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7807989, HC$15. MF$7.50. 177 p. 1977.

Research was carried out with esophageal, nasopharyngeal, and abdominal intragastric (IG) techniques in rats to assess which was the most suitable for animal studies of drug dependence. The esophageal method was found superior to the others in surgical trauma and lack of induction of undesirable behavioral or physiological effects, as well as least discomfort, hemorrhage, and ulceration. To provide data on the effectiveness of the esophageal method for the study of drug dependence, research was carried out on self-administration of morphine. Experiments examined dose response relationships, tolerance, deprivation, and satiation. Results are discussed in terms of the superiority of the IG esophageal method and the usefulness of this technique for the study of variables associated with drug dependence. (Journal abstract modified)

003438 Spector, S.; Felix, A.; Semenuk, G.; Finberg, J. P. M. Department of Physiological Chemistry and Pharmacology, Roche Institute of Molecular Biology, Nutley, NJ 07110 **Development of a specific radioimmunoassay for acetylcholine.** Journal of Neurochemistry (Oxford). 30(4):685-689, 1978.

The synthesis of an acetylcholine (ACh)-like immunogen and its use in the production of antibodies specific to ACh is described. Cross-reactivity of anti ACh antibody to choline was only 0.1% of that to ACh. Insignificant cross reaction to acetate and phosphorylcholine occurred, enabling use of these antibodies in a radioimmunoassay for determination of endogenous ACh levels. Significant cross reactivity of the antibody to succinylcholine, decamethonium, dimethylphenylpiperazinium, carbachol, and butyrylcholine was observed. The correlation coefficient for determination of endogenous ACh by bioassay and radioimmunoassay was 0.994. ACh levels by radioimmunoassay in brain areas of rats killed by microwave irradiation were: striatum, 77.8; cortex, 28.8; hippocampus, 25.4; midbrain, 47; and hypothalamus, 25nM/g. 21 references. (Author abstract)

003439 Spiegel, Herbert E.; Symington, Julia; Savulich, Anne. Hoffman-La Roche, Inc., Kingsland Street, Nutley, NJ 07110 **The stability and reliability of radioimmunoassays for clonazepam, diphenylhydantoin and phenobarbital in blood, serum or plasma.** Research Communications in Chemical Pathology and Pharmacology. 19(2):271-280, 1978.

Interference studies were conducted to find a way of preserving the in vitro drug levels of clonazepam, diphenylhydantoin, and phenobarbital when plasma could not be maintained in a refrigerated or frozen state. After a series of experiments established the stability of each of the three anticonvulsant drugs in plasma and whole blood samples under refrigerated and frozen states, a series of interference experiments showed that clonazepam, diphenylhydantoin and phenobarbital were stable for up to a week at 37 degrees centigrade in plasma containing K3EDTA and NaN3. 4 references.

003440 Stone, Eric A. Millhauser Laboratories, Department of Psychiatry, New York University School of Medicine, 550 First Avenue, New York, NY 10016 **Improved polyethylene intracerebroventricular cannulas for rats.** Physiology & Behavior. 20(5):657-659, 1978.

Modifications of a previously published method for construction and implantation of polyethylene cannulas for injection into the lateral cerebral ventricle of the rat are described. With the improved cannulae construction and modified injection technique, the use of stereotaxic equipment for restraint is eliminated. The new techniques allow either single or repeated injections to be given without handling the unanesthetized animals. The technique is suitable for a variety of behavioral and biochemical studies, including those with animals made irritable by CNS lesions. 4 references. (Author abstract modified)

003441 Walter, D. S.; Dettmar, P. W.; Taylor, K.; Shilcock, G. M.; Cowan, A. Department of Pharmacology, Reckitt and Colman, Pharmaceutical Division, Dansom Lane, Hull HU8 7DS, England **Routine measurement of homovanillic acid in rat brain by gas-liquid chromatography.** Journal of Neurochemistry (Oxford). 30(4):929-931, 1978.

A simple method for routine measurement of homovanillic acid (HVA) in brain by gas liquid chromatography is described. Using this method, rat striatal HVA concentrations were found to be significantly reduced after administration of haloperidol and significantly increased after administration of apomorphine. Reductions in striatal HVA were also detected after administration of ascorbic acid or citric acid vehicle. Results indicate the importance of using properly matched control animals prior to statistical evaluation of neuropharmacological data. 16 references.

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

003442 Forsman, Anders; Ohman, Rolf. Psychiatric Department III, Lillhagen's Hospital, S-422 03 Hisings Backa, Sweden **On the objective evaluation of haloperidol effects in man: a pilot study.** Current Therapeutic Research. 24(2):179-192, 1978.

Various facets of drug-induced side-effects originating in the extrapyramidal system were evaluated quantitatively after administration of haloperidol (3 to 90mg per day) to 12 chronic schizophrenic inpatients. Neurometabolic effects were studied by determining acid neurotransmitter metabolites in the cerebrospinal fluid (CSF), as were hypothalamic effects by measuring serum prolactin levels. The results indicate a decreased spontaneous motility at high serum concentrations of haloperidol. The total flow of saliva did not change significantly. The serum prolactin concentration increased with rising serum levels of haloperidol until a final leveling off at individually varying values. The results are compatible with the predominantly central dopamine receptor blocking properties of haloperidol and with its lack of at least peripheral anticholinergic effects. 32 references. (Author abstract modified)

003443 Gamkrelidze, S. A.; Putkaradze-Gamkrelidze, N. A. Institute of Psychiatry, u. Asatriani 10 Tbilisi 77, USSR **Pirroxan in the treatment of the neurovegetative component of the depressive syndrome.** Activitas Nervosa Superior (Praha). 20(1):67-68, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the use of Pirroxan, a new drug, in the treatment of the neurovegetative component of the depressive syndrome is discussed. Pirroxan was prescribed to 111 depressive outpatients with expressive somatic complaints (visceral spasms, constipation, meteorism, tachycardia, and cardiac fears) in conjunction with antidepressants. Results indicate that Pirroxan does not posses a true antidepressive potency, but by relieving unpleasant neurovegetative components of the depressive syndrome, it potentiates the antidepressive activity of thymoanaleptics.

003444 Holden, Constance. no address **Coca proposed as prescription drug.** Science. 199(4334):1184, 1978.

Andrew Weil, an ethnopharmacologist, has announced plans to ask the Food and Drug Administration for permission to test coca, from which cocaine is derived, on human subjects. Weil contends that consuming the natural plant extract is safer than many tranquillizers and antidepressants. Although Freud originally felt cocaine would be a good antidepressant he later emphasized its use in the treatment of neurasthenia and opiate addiction. That Weil's proposal has not stirred considerable controversy is an indication of the increasing sophistication of drug research and changing public attitudes toward the morality of drug use and toward established medicine. Psychiatrists David Musto and Lester Grinspoon suggest that while coca may be a good mood elevator it would be ineffective in the treatment of serious depression and that other benefits or uses of the drug would be too marginal to justify increasing the availability of such an attractive drug of abuse.

003445 Kelly, John T.; Zimmerman, Robert L.; Schiele, Burtrum C. Dept. of Psychiatry, University of Minnesota Hospitals, Box 381 Mayo Memorial Building, 420 Delaware St. SE, Minneapolis, MN 55455 **The treatment of anxiety with a polyfluorinated benzodiazepine derivative.** Neuropsychobiology (Basel). 4(5):283-287, 1978.

Following 4 weeks of treatment with ORF-8063, a polyfluorinated benzodiazepine derivative, eight hospitalized patients manifesting a primary pathology of anxiety showed marked general improvement. Two others were treated for shorter periods of 9 and 14 days. Mean optimal dosage was 66.5mg. The five instruments used to measure therapeutic effect showed pretreatment to posttreatment change with high level of statistical significance in several of the pathological factors. When measures of change are considered, patients showed more improvement related to psychic than somatic components of anxiety. Change data also indicates more patient improvement in anxiety than depression. Side-effects reported most were dizziness, faintness, and insomnia, which were reported in eight patients. Six patients noted drowsiness, and four noted excitement. Five persons tolerated optimum dosages with no extreme reactions; five others (including the two subjects who terminated treatment early) were unable to maintain optimum dosages because of side-effects. 6 references. (Author abstract)

003446 Pallegoix, M.; Rogowski, J.-C.; Atalla, S.; Bonnaffoux, D. Centre Psychotherapique du Jura, F-39108 Dole-Saint-Ylie, France **/Contribution of the use of 1035M.D. in a psychiatric ward for adults, its activity on the direct and side-effects of neuroleptics./** Contribution a l'emploi du 1035 M.D. dans un service de psychiatrie adulte, son activite sur les effets directs et secondaires des psychotropes. Psychologie Medicale (Paris). 10(3):563-567, 1978.

A 7 month study of 1035M.D. attempted to clinically confirm the improvement of nutritional exchanges and determine the effect of 1035M.D. on correcting various side-effects of neuroleptics. Both parts of the study involved 30 hospitalized patients, 20 female and 10 male. Subjects in the first part were given a uniform dosage of two capsules three times a day. The results show that 1035M.D. is effective in treating certain psychological deficiencies and in maintaining normal blood pressure. It was also found that 1035M.D. helps activate neuron metabolism and corrects various disorders caused by neuroleptics. 7 references. (Journal abstract modified)

003447 Peterson, George R.; Blackwell, Barry; Hostetler, Russell M.; Kuzma, Ronald; Adolphe, Allen. Department of Pharmacology, Wright State University School of Medicine, Dayton, OH 45435 **Anticholinergic activity of the tricyclic antidepressants despiramine and doxepin in nondepressed volunteers.** Communications in Psychopharmacology. 2(2):145-150, 1978.

In a continuation of systematic comparisons of tricyclic antidepressant drugs, desipramine and doxepin were compared in normal, nondepressed female volunteers with regard to anticholinergic properties (measured by inhibition of salivary flow) and central effects, such as sedation (measured by the Clyde Mood Scale). Doxepin and desipramine at 50 and 100 mg produced depression of salivary flow compared to placebo. The 100 mg dose of doxepin caused greater ingibition of salivation than the corresponding dose of desipramine. CNS effects like sedation were significantly more pronounced with doxepin than with desipramine. In addition, more voluntary complaints concerning adverse effects were recorded for doxepin than for desipramine. 8 references. (Author abstract modified)

003448 Yassa, Ramzy; Nair, Vasavan; Schwartz, George. Douglas Hospital Centre, 6875 LaSalle Boulevard, Montreal, Quebec, Canada H4H 1R3 **Treatment of leukopenia with lithium carbonate: a preliminary report.** American Journal of Psychiatry. 135(11):1423-1424, 1978.

Published reports that lithium treatment has been associated with hematologic changes in the direction of leukocytosis prompted the administration of lithium carbonate to three chronic schizophrenic patients who consistently showed leukopenia. There was a consistent and significant increase in total white blood cell count as well as in the neutrophil count in these patients during the 3 weeks of lithium administration, reaching a maximum by the end of the third week. After discontinuation of lithum, there was a steady decline to baseline levels. The white blood cell increase was not correlated with serum lithium levels. 10 references.

08 DRUG TRIALS IN SCHIZOPHRENIA

003449 Alpert, Murray; Friedhoff, Arnold J.; Marcos, Luis R.; Diamond, Florence. Dept. of Psychiatry, New York University School of Medicine, 550 First Ave., New York, NY 10016 **Paradoxical reaction to L-dopa in schizophrenic patients.** American Journal of Psychiatry. 135(11):1329-1332, 1978.

In an investigation of the dopamine hypothesis of schizophrenia, paradoxical reactions to L-dopa in schizophrenic patients were found. Following administration of 6g of L-dopa to eight schizophrenic patients and 750mg of chlorpromazine to seven schizophrenic patients, chlorpromazine showed only a modest advantage over L-dopa and only on some Brief Psychiatric Rating Scale factor scores, and at maximum dosage the thought disturbance factor score in the L-dopa group was not worse than at baseline. Results suggest that L-dopa is associated more with toxic than with schizophreniform symptoms and that there is adaptation to its effects. 21 references. (Author abstract modified)

003450 Branchey, Marc H.; Lee, J. Hillary; Amin, Ramesh; Simpson, George M. Dept. of Mental Hygiene, Rockland Research Institute, Orangeburg, NY 10962 **High- and low-potency neuroleptics in elderly psychiatric patients.** Journal of the American Medical Association. 239(18):1860-1862, 1978.

The efficacy and side-effects of a low potency neuroleptic, thioridazine hydrochloride, and those of a high potency neuroleptic, fluphenazine hydrochloride, were compared in 30 elderly chronic schizophrenic patients. Through a crossover design, each patient received both drugs with an intervening washout period. Although both drugs produced a similar degree of improvement, their side-effects differed. Fluphenazine caused slightly more extrapyramidal effects than thioridazine, though few occurred with use of either drug. Thioridazine caused weight gain, blood pressure decreases, and ECG changes. High potency neuroleptic agents appear to be the drugs of choice for elderly schizophrenic patients. 10 references. (Author abstract)

003451 Chouinard, Guy; Annable, Lawrence; Young, Simon N.; Sourkes, Theodore L. Allan Memorial Institute McGill Univeristy, Montrial, Quebec, Canada **A controlled study of tryptophan-benserazide in schizophrenia.** Communication in Psychopharmacology. 2(1):21-31, 1978.

The effects of tryptophan-benserazide and chlorpromazine on schizophrenic patients were compared in a double-blind controlled study of 32 patients from the Louis-H. Lafontaine Hospital. The patients were evaluated by the Brief Psychiatric Rating Scale, Nurses' Observation Scale for Inpatient Evaluation, Extrapyramidal Symptom Rating Scale, and Treatment Emergent Syptoms along with laboratory tests and electrocardiograms. The results indicate that tryptophan-benserazide was less efficacious than chlorpromazine as regards relapse rate, use of supplementary chlorpromazine, and symptom rating scales. It had a beneficial effect on the symptoms of depressive mood and guilt feelings, and had little or no effect on the extrapyramidal system. Although these results indicate that the antipsychotic action of tryptophan-benserazide is less than the clinical effect obtained with phenothiazines, the fact that it did not affect the extrapyramidal systems also indiates a potential future therapeutic value. 22 references.

003452 Crow, T. J.; Johnstone, Eve C.; Longden, A. J.; Owen, F. Division of Psychiatry, Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex, England **Dopaminergic mechanisms in schizophrenia: the antipsychotic effect and the disease process.** Life Sciences (Oxford). 23(6):563-567, 1978.

In a paper presented at the Janssen Symposium on Receptors of Dopamine Antagonists -- New Biochemical Approaches, held in Beerse, Belgium, July 1978, the hypothesis that antipsychotic drugs act by blocking dopamine (DA) receptors is discussed. A controlled trial of the isomers of flupenthixol in acute schizophrenics showed that only the alpha-isomer possessed antipsychotic activity, which is consistent with the hypothesis that DA receptor blockade is the only requirement for therapeutic activity. However, the onset of the therapeutic effect was slow; clinical improvement was not evident until at least 2 weeks after the establishment of DA receptor blockade, indicated by increased prolactin secretion. In postmortem brain tissue, DA turnover was not elevated in patients with schizophrenia. However, receptor density (assessed by spiroperidol binding) was significantly increased in schizophrenic brains, including those of five patients who had not received neuroleptic medication for at least one year before death. 6 references. (Author abstract modified)

003453 Dencker, S. J.; Johansson, R.; Lundin, L.; Malm, U. Department 2, Lillhagen Hospital, Box 3005, S-422 03 Hisings Backa 3, Sweden **High doses of fluphenazine enanthate in schizophrenia.** Acta Psychiatrica Scandinavica (Kobenhavn). 57(5):405-414, 1978.

A controlled study of 12 schizophrenics refractory to ordinary doses of neuroleptics was made which indicates that treatment with fluphenazine enanthate in higher doses than normal (10-20 times higher) might give reduction in psychopathology beyond what can be obtained with normal doses. In four patients the symptom reduction on high doses was pronounced. It was found that the high fluphenazine plasma levels demonstrated did not increase extrapyramidal and general side-effects. The results indicate that a non responding patients may need a higher plasma level of a neuroleptic than the average patient. 13 references. (Author abstract)

003454 Dom, R.; De Mesmaecker, L.; Van Den Broucke, M.; Van Hest, T.; Baro, F. Psychiatric University Centre, St. Kamillus, B-3043 Bierbeek, Belgium **Maintenance treatment of chronic schizophrenic patients. A study with the long-acting thioxanthene derivative, cis(Z)-clopenthixol decanoate-sordinol depot.** Acta Psychiatrica Scandinavica (Kobenhavn). 57(4):299-304, 1978.

The clinical effect of clopenthixol decanoate was assessed in a 5 month controlled study including 21 hospitalized chronic schizophrenic patients. The ratings were done with Brief Psychiatric Rating Scale (BPRS), Nurses Observation Scale for Inpatient Evaluation (NOSIE-30), the two psychological tests of WAIS and Grunbaum, and the rating scale of Simpson & Angus to assess extrapyramidal side-effects. Clopenthixol decanoate was found an effective and long-acting antipsychotic compound with few autonomic and neurological side effects. Compared with previous maintenance treatment it also shows a positive influence on depression and facilitation of the social adaptation of the patients. 10 references. (Author abstract)

003455 Falloon, I.; Watt, D. C.; Shepherd, M. Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England **The social outcome of patients in a trial of long-term**

continuation therapy in schizophrenia: pimozide vs. fluphenazine. Psychological Medicine (London). 8(2):265-274, 1978.

The short-term and long-term social outcome of 41 schizophrenic patients on continuation therapy treated in a double-blind trial of pimozide (oral) and fluphenazine decanoate (injection) following discharge after a clearly defined schizophrenic breakdown is evaluated. Social adjustment of the patients at home was assessed by interviews with patients and their relatives by means of the Medical Research Council Social Performance Schedule at 1 month and at 12 months later, or at the time of relapse. Patients on pimozide were significantly more favorably rated on aspects of sociability, use of leisure activity, warmth of personal relationships, household tasks, and child-drearing. In conclusion, results support the claim that pimozide enables community based schizophrenics to function more effectively in their social environment than do the long-acting phenothiazines. 21 references. (Author abstract modified)

003456 Frangos, H.; Zissis, N.; P. Leontopoulos, I.; Diamantas, N.; Tsitouridis, S.; Gavrilil, I.; Tsolis, K. 39 Mousson Street, Pal. Phaleron, Athens, Greece **Double-blind therapeutic evaluation of fluspirilene compared with fluphenazine decanoate in chronic schizophrenics.** Acta Psychiatrica Scandinavica (Kobenhavn). 57(5):436-446, 1978.

A comparison study of the antipsychotic action as well as the side-effects of the long acting neuroleptics fluspirilene and fluphenazine decanoate was made under double-blind conditions. Fifty chronic schizophrenics were randomly assigned to a 61 week treatment either with fluspirilene or with fluphenazine decanoate. Fluphenazine decanoate caused more side-effects and the difference between the two groups was statistically significant in tremor, severe extrapyramidal effects, and parkinsonism. More patients in the fluspirilene group (nine patients) compared with only three in the fluphenazine decanoate group remained free of side-effects during the whole trial. Fluspirilene proved an equally potent neuroleptic with fluphenazine decanoate although statistically significant improvement has been obtained in more items of the scale in the fluspirilene group. Although Clinical Global Impressions of the investigators and the nursing personnel favored fluspirilene, the differences between the two groups were not statistically significant. 25 references. (Author abstract modified)

003457 Gibson, Alan C. St. Ann's Hospital, Haven Road, Canford Cliffs, Poole, Dorset BH13 7LN, England **Sodium valproate and tardive dyskinesia.** British Journal of Psychiatry (London). 133(July):82, 1978.

Twenty five schizophrenic patients with tardive dyskinesia, given 600 mgs sodium valproate daily with their neuroleptic medication, were studied. The results show that after one month there was no change in their signs, as judged by a panel of nine, viewing films of them taken before and at the end of this treatment. It is concluded that the treatment was unsuccessful. 2 references. (Author abstract modified)

003458 Horrobin, David F. Clinical Research Institute, 110 Pine Ave. West, Montreal, Quebec, Canada **Dopamine supersensitivity, endorphin excess, and prostaglandin E1 deficiency: three aspects of the same schizophrenic elephant.** Schizophrenia Bulletin. 4(4):487-488, 1978.

A hypothesis relating prostaglandin El (PGE1) deficiency to schizophrenia is presented. The hypothesis is consistent with the importance of prolactin stimulating properties in currently used antipsychotic drugs, the effect of prolactin on PGE1 synthesis, and the deficiency of PGE1 regulation in schizophrenia platelets. The hypothesis is related to theories implicating dopamine and endorphins in the etiology of schizophrenia. It is reported that a clinical trial in chronic schizophrenics suggested the possible therapeutic efficacy of penicillin, a drug without dopamine blocking actions which stimulates PGE1 synthesis directly. 11 references. (Author abstract modified)

003459 Iqbal, M. Javed; Young, Michael A.; Charles, Jesse; Elgart, Beltran; Von Grieff, Herman; Simpson, George M. Bergen Pines County Hospital, Paramus, NJ 07652 **A long term comparative trial of penfluridol and fluphenazine decanoate in schizophrenic outpatients.** Journal of Clinical Psychiatry. 39(4):375-376, 379, 1978.

The efficacy of penfluridol and fluphenazine decanoate in the maintenance therapy of schizophrenic outpatients was compared in a double-blind, investigation of 38 subjects. Penfluridol, a diphenylbutylpiperidene derivative, is a new long-acting neuroleptic, administered orally once a week. Both drugs were found to be equally successful in maintaining the patients, and the incidence and frequency of side-effects were similar. 11 references. (Author abstract modified)

003460 Johnstone, Eve C.; Crow, T. J.; Frith, C. D.; Carney, M. W. P.; Price, J. S. Division of Psychiatry, Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex, HA1 3 UJ, England **Mechanism of the antipsychotic effect in the treatment of acute schizophrenia.** Lancet (London). 1(8069):848-851, 1978.

A comparison of the alpha-isomer of flupenthixol to beta-flupenthixol and placebo in the treatment of acute schizophrenia is presented. The alpha-isomer was found to be considerably more effective in blocking delusions, hallucinations, and thought disorders, and was most effective in the third and fourth weeks of the study. Subjects were 45 volunteers, all shizophrenic and over 16 years of age. Findings are consistent with the hypothesis that dopamine receptor blockade is the only requirement for the antipsychotic activity, and suggests that the antipsychotic effect occurs only in those patients with typically schizophrenic illnesses but may be limted to positive symptoms. 22 references.

003461 Jus, A.; Gautier, J.; Villeneuve, A.; Jus, K.; Pires, P.; Gagnon-Binette, M.; Fortin, C. Dept. of Psychiatry, Centre Hospitalier Robert-Giffard, 2601, de la Canardiere, Beauport, Quebec G1J 2G3, Canada **Pharmacokinetic interaction between amitriptyline and neuroleptics.** Neuropsychobiology (Basel). 4(5):305-313, 1978.

The influence of amitriptyline on the plasma level of various neuroleptics was studied in 25 chronic schizophrenic patients for 20 weeks. Patients remained on their former neuroleptic medication for the first 4 weeks, with amitriptyline added for 12 subsequent weeks, and then withdrawn during the last 4 weeks when only the neuroleptic medication was continued unchanged. The plasma level of neuroleptics was assayed by gas liquid chromatography once weekly throughout the study. The amitriptyline plasma level was also evaluated once weekly during the 12 weeks of its administration. The mean neuroleptic plasma values for each 4 week period were pooled together in three groups: aliphatic, piperidine, and piperazine phenothiazine derivatives. Amitriptyline provoked some increase of the plasma level of all phenothiazine derivatives. This augmentation was significant only transitorily. The putative mechanisms of this neuroleptic tricyclic antidepressant interaction are discussed. 19 references. (Author abstract)

003462 Lindholm, Halvar; Gullberg, Bo; Ohman, Annika; Sedvall, Goran. Laboratory of Experimental Psychiatry, Department of Psychiatry, Karolinska Hospital, S-104 01, Stockholm, Sweden **Effects of perphenazine enanthate injections on prolactin levels in plasma from schizophrenic women and men.** Psychopharmacology (Berlin). 57(1):1-4, 1978.

Levels of prolactin in plasma were determined in schizophrenic men and women after intramuscular injection of 50mg to 150mg perphenazine enanthate. A dose related increase in prolactin levels was observed in both sexes following administration of the neuroleptic drug. The effect was significant for 2 days in men and for 9 days in women. Treatment with biperiden did not influence the effect of perphenazine enanthate on prolactin levels. Since the secretion of prolactin from the pituitary gland is regulated by hypothalamic dopamine neurons, it is concluded that perphenazine enanthate, in therapeutic doses, induces a small but significant blockade of central dopamine receptors. 16 references. (Author abstract modified)

003463 Martin, Ian C. A. Memorial Hospital, Darlington, England **Clinical parable: mirthless merry-go-round.** Nursing Times (London). 74(34):1426-1427, 1978.

The case history of a patient who responded to the depot release antipsychotic drug phenothiazine after a long history of relapses is described. Previously, it had been reported that one of the bigest obstacles to the successful treatment of schizophrenics had been the fact that many patients lacked the determination or insight to keep taking their oral medication. In addition, a number of patients were found to be unable to absorb these compounds when given by mouth because they have a mechanism in the wall of their gastrointestinal tract which actively destroys these drugs before they can reach the blood stream or brain. With the advent of injectible phenothiazine, patients such as the one described in the case history, may be able to function more normally and lead highly constructive lives.

003464 Masiak, Marek W. Institute of Psychiatry, Warsaw, Poland **Contemporary views on the role of neuroleptics in the treatment of schizophrenia and their action in the central nervous system.** African Journal of Psychiatry (Lagos). 4(1,2):1-5, 1978.

A complex method of treatment of schizophrenic patients which takes into account the role of neuroleptics and their action in the nervous system is presented. Three aspects of the drug treatment of schizophrenia are discussed: 1) evaluation of drug treatment by comparison with nonbiological methods, 2) individualization of the treatment, and 3) mechanism of action of neuroleptics and pathogenesis of schizophrenia. The dopamine hypothesis of schizophrenia is examined. An experiment involving a group of simple schizophrenic patients characterized by social and motor inactivity indicated a positive reaction to haloperidol treatment but not to chlorpromazine. The results are interpreted in relation to the dopaminergic system. 12 references.

003465 Nestoros, J. N.; Lehmann, H. E.; Ban, T. A. Department of Research in Anaesthesia, McGill University, 3655 Drummond St., Montreal, P. Q. H3G 1Y6, Canada **Butaclamol in the treatment of schizophrenia. A standard-controlled clinical trial.** International Pharmacopsychiatry (Basel). 13(3):138-150, 1978.

A 16 week, standard controlled, double-blind study was conducted to compare the efficacy of butaclamol with that of fluphenazine in the treatment of 24 newly admitted schizophrenic patients. Statistically significant improvement occurred in the entire sample as measured by the Psychophathological Assessment Scale (PAS) and the Brief Psychiatric Rating Scale (BPRS): improvements were found in anergia, hostile/suspiciousness, activation, and thought disturbance scores of the BPRS and in nine of 12 factors of the PAS. There were no statistically significant differences between the scores of the two treatment groups on the total or factor scores of either scale during the course of the clinical trial. The most frequent adverse effects in the butaclamol group were rigidity, akathisia, and excitement/agitation. In the fluphenazine group adverse effects included insomnia, decreased motor activity, and tremor. It is concluded that butaclamol exerts potent neuroleptic effects on schizophrenic patients. 14 references. (Author abstract)

003466 Odejide, A. O. Department of Psychiatry, University College Hospital, Ibadan, Nigeria **Outpatient maintenance of chronic schizophrenic patients with fluphenazine decanoate (Modecate): Ibadan experience.** African Journal of Psychiatry (Lagos). 4(1,2):37-41, 1978.

A 6 month assessment is presented of 99 chronic schizophrenic patients in Nigeria who were stabilized and maintained on a long acting phenothiazine, Modecate. Using the clinical global rating and the Brief Psychiatric Rating Scale, 92% of the patients were found to be well maintained outside the hospital throughout the study period. A wider use of the drug is suggested. Community management of chronic schizophrenics using Modecate is recommended as a solution to reducing the rate of defaulting. 12 references. (Author abstract)

003467 Quitkin, Frederic; Rifkin, Arthur; Kane, John; Ramos-Lorenzi, Jorge R.; Klein, Donald F. New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Long-acting oral vs injectable antipsychotic drugs in schizophrenics: a one-year double-blend comparison in multiple episode schizophrenics.** Archives of General Psychiatry. 35(7):889-892, 1978.

A total of 60 patients meeting the criteria established for schizophrenia who attained a clinical plateau following hospital discharge were examined to compare the efficacy of antipsychotic drugs administered orally and hypodermically. The subjects were randomized to receive for one year either penfluridol, 20 to 160mg orally once every week, or fluphenazine decanoate, .5to 3.75ml every two weeks. The relapse rate for both treatments was low and equal. The rate of recurrence of psychosis for patients receiving penfluridol was 7%, and for those receiving fluphenazine decanoate 10%. A retrospective comparison of the penfluridol group was made to a similar group of patients assigned to placebo in an earlier study. Placebo treated patients had a relapse rate of 68%. Penfluridol patients had statistically fewer psychotic relapses. The study demonstrates the feasibility of using an oral, long-acting antipsychotic agent. If the question of its carcinogenicity were resolved, it would be a useful psychopharmacologic addition in the treatment of outpatient schizophrenics. 10 references. (Author abstract modified)

003468 Reynolds, Thomas D.; London, Wayne P.; Yorke, James A. St. Elizabeth's Hospital, William A. White Division, Washington, DC 20032 **Behavioral rhythms in schizophrenia.** Journal of Nervous and Mental Disease. 166(7):489-499, 1978.

Behavioral rhythms in schizophrenia, manifested as repetitive talking, pacing or rocking behaviors, are discussed. Daily behavioral observations were made for several years on 10 male schizophrenic patients and on three male patients with organic brain disorders. Analysis of these data showed strong cyclic components in the five schizophrenic patients with predominantly hebephrenic symptomatology. Period lengths noted were about 2 days, 5 to 6 days, 30 days, and a longer cycle of 40 to 100 days duration. Antipsychotic medications appear to have a suppressant effect, but tricyclic antidepressants may enhance preexisting rhythms. It is concluded that data from this experiment may permit the development of quantitative methods for exploring particular hypotheses about the underlying bases of some forms of schizophrenia. 11 references. (Author abstract modified)

003469 Rivera-Calimlim, Leonor; Gift, Tom; Nasrallah, Henry A.; Wyatt, Richard Jed; Lasagna, Louis. Dept. of Pharmacology, University of Rochester School of Medicine and Dentistry,

Rochester, NY 14642 **Low plasma levels of CPZ in patients chronically treated with neuroleptics.** Communications in Psychopharmacology. 2(2):113-121, 1978.

To explore the relationships among chronicity of illness, intensity and duration of prior neuroleptic treatment, and plasma levels of chlorpromazine, (CPZ) data from 133 schizophrenic patients was statistically analyzed. A multiple regression analysis with covariance was performed with plasma concentrations as the dependent variable and with hospital, years of illness, years of prior neuroleptic treatment, CPZ dose, presence or absence of anticholinergic medications as the independent variables. The analysis indicates that, keeping all independent variables constant, the best predictor for plasma concentrations is the dose of CPZ and that plasma concentrations decrease with an increase in the duration of treatment. The model predicts that with prolonged CPZ treatment, the plasma concentration will diminish by 5-10% per year. 14 references. (Author abstract modified)

003470 Rompel, H.; Segal, H. Stikland Hospital, Bellville, South Africa **A comparison of the relative efficacy of Serenace and chlorpromazine in the treatment of chronic schizophrenics.** Journal of International Medical Research (Northampton). 6(2):126-132, 1978.

A study designed to assess the relative efficacy of chlorpromazine and Serenace in the control of chronic schizophrenics is described. A total of 25 cases were selected for the study and were randomly allocated to treatment. The condition of the patients was assessed at fortnightly intervals over the 8 week duration of trial period. No significant differences in side-effects emerged in patients on chlorpromazine and Serenace in the dosages administered. Results indicate that the statistically significant trends all show a superiority of Serenace above chlorpromazine which is in accord with the clinical picture. (Author abstract)

003471 Simon, Pierre; Fermanian, Jacques; Ginestet, Daniel; Goujet, Michele-Annie; Peron-Magnan, Pierre. Department of Clinical Pharmacology, Faculte de Medecine, Pitie-Salpetriere 91, Boulevard de l'Hopital, 75634 Paris Cedex 13, France **Standard and long-acting depot neuroleptics in chronic schizophrenics: an 18-month open multicentric study.** Archives of General Psychiatry. 35(7):893-897, 1978.

An 18-month open study to compare standard neuroleptics and long-acting depot neuroleptics to determine the best therapy available through current psychiatric practices is reported. Thirty French psychiatrists from 15 different wards participated in the experiment. One hundred eighty one chronic schizophrenic patients were randomly assigned to receive one of the following three treatments: 1) standard neuroleptics, 2) pipotiazine palmitate, or 3) fluphenazine decanoate. Criteria used for evaluation were an overall clinical evaluation by a psychiatrist, a Brief Psychiatric Rating Scale, and a Nurse's Observation Scale for Inpatient Evaluation. No significant difference was observed between the three groups in drug effectiveness or tolerance. 13 references. (Author abstract)

003472 Singh, A. N.; Saxena, B.; Nelson, H. L. Fennell Programme, Hamilton Psychiatric Hospital, Hamilton, Ontario, Canada **A controlled clinical study of trazodone in chronic schizophrenic patients with pronounced depressive symptomatology.** Current Therapeutic Research. 23(4):485-501, 1978.

Trazodone hydrochloride was compared to placebo as an adjuvant medication to basal phenothiazine therapy in a double-blind clinical trial in chronic hospitalized depressed schizophrenic patients. It was shown to be superior to placebo in its antidepressant action. Trazodone was well tolerated and its administration was associated with minimal side-effects. In addition, trazodone was pharmacologically compatible with phenothiazine medication. Maximum therapeutic effects were achieved with the dosage of 300mg per day of trazodone. 29 references. (Author abstract)

003473 Singh, Man Mohan; Kay, Stanley R. Veterans Administration Hospital, 1030 Jefferson Avenue, Memphis, TN 38104 **Therapeutic antagonism between anticholinergics and neuroleptics: possible involvement of cholinergic mechanisms in schizophrenia.** Schizophrenia Bulletin. 4(1):3-6, 1978.

A reply to criticisms by Meltzer and Stahl (1976) of earlier research by Singh and Kay (1975) and Singh and Smith (1973) in which anticholinergic agents were added to ongoing neuroleptic treatment is presented. It is argued that the suggested analysis of variance for repeated measures for the three treatment phases is inappropriate because of the expected carryover effects from continuous neuroleptic treatment. The multivariate analysis of various parameters seems unsuitable because homogeneity of covariance can not be ensured due to the heterogeneity of schizophrenia and the diversity of factors represented in psychopathology measures. The results of recent parametric and nonparametric analyses of combined data from three studies are summarized to show that the significant effects clearly point to a therapeutic antagonism between anticholinergics and neuroleptics. It is suggested that cholinergic neurons may be part of some crucial discriminative control mechanisms in the brain organization that are ineffective in schizophrenia and lead to a relative overactivity of the opposing catecholaminergic neurons in the midbrain/limbic circuitry which promote repetition of behaviors in goal directed activity. 23 references.

003474 Tamminga, Carol A.; Schaffer, Martin H.; Smith, Robert C.; Davis, John M. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **Schizophrenic symptoms improve with apomorphine.** Science. 200(4341):567-568, 1978.

The effects of apomorphine, a dopamine receptor agonist, on schizpohrenic symptoms were studied in 18 chronic schizophrenic patients who received subcutaneous doses of apomorphine and a placebo in separate trials. A significant improvement in psychotic symptoms occurred after apomorphine as compared to placebo. Results are interpreted as a consequence of presynaptic dopamine receptor activation by apomorphine with a subsequent decrease in dopamine mediated neural transmission. 13 references. (Author abstract)

003475 Tamminga, Carol A.; Crayton, John W.; Chase, Thomas N. Department of Psychiatry, University of Chicago, 950 E. 59th St., Chicago, IL 60637 **Muscimol: GABA agonist therapy in schizophrenia.** American Journal of Psychiatry. 135(6):746-747, 1978.

The effects of muscimol, an analogue of gamma-aminobutryic acid (GABA), on psychotic symptoms of chronically hospitalized schizophrenics were investigated. Muscimol was administered to six patients in a controlled, double-blind study. At maximum dose levels, deteriorations in scores for confusion, affect, and thought disorder were observed. All subjects showed diffuse myoclonic twitching or somnolence. The results do not support the hypothesis that pharmacologic augmentation of GABA transmission will improve symptoms of schizophrenia. 10 references.

003476 Woggon, B.; Angst, J. Psychiatrische Universitatsklinik Zurich, Forschungsdirektion, CH-8000 Zurich, Switzerland **Double-blind comparison of bromperidol and perphenazine.** International Pharmacopsychiatry (Basel). 13(3):165-176, 1978.

The effects and side effects of bromperidol and perphenazine were compared in a clinical double-blind study of 40 newly hos-

pitalized schizophrenic patients. Assessments were made on days 0, 2, 5, 10, 20, and 30. Laboratory tests and electrocardiograms were performed before and after treatment. A therapeutic effect mean dose of 6mg was found for bromperidol, and of 20mg for perphenazine. Both substances were associated with autonomic and extrapyramidal side effects, and in a few patients, temporary fatigue. The employed dosages caused no strong sedation. Both drugs can be described as highly potent and well tolerated antipsychotic drugs. A stronger efficacy and earlier onset of action was observed with bromperidol. This superior effect can not be explained by the higher dosage as compared with perphenazine; as both substances showed a similar severity of extrapyramidal side effects, and dosages of both substances was established individually for each patient dependent on effects and side effects. 10 references. (Author abstract modified)

003477 Wyatt, Richard J.; Potkin, Steven G.; Walls, Philip D.; Nichols, Anna; Carpenter, William; Murphy, Dennis. Laboratory of Clinical Psychopharmacology, NIMH, Bethesda, MD **Clinical correlates of low platelet monoamine oxidase in schizophrenic patients.** In: Akiskal, H., Psychiatric diagnosis. New York, SP Medical & Scientific Books, 1978. 493 p. (p. 279-297).

Preliminary data on platelet monoamine oxidase (MAO) activity are presented from adult patients with the diagnosis of schizophrenia and from other groups. Platelet MAO activity was studied in 62 male and 15 female chronic schizophrenic patients. Both males and females had significantly lowered platelet MAO activity as compared with normal controls (p was less than 0.001 in both cases). Platelet MAO activity was examined also in 9 monozygotic and 10 dizygotic normal twins, in monozygotic twins discordant for schizophrenia, and in first degree nonschizophrenic relatives of index schizophrenics. It is concluded that MAO activity is low in some schizophrenics, especially chronic paranoid schizophrenics. The deficit appears to be at least partly under genetic control, and it does not seem to be present in acute schizophrenics. There is a tendency for platelet MAO activity to be lower when paranoid symptoms are present. 28 references.

003478 Ziemba, Thomas; Meltzer, Herbert Y.; Davis, John M. Laboratory of Biological Psychiatry, Illinois State Psychiatric Institute, Chicago, IL 60612 **Do anticholinergics antagonize antipsychotic drug action?** Schizophrenia Bulletin. 4(1):7-12, 1978.

The advantages of using a split plot repeated measures analysis of variance to test the hypothesis that anticholinergics interfere with the therapeutic effects of chlorpromazine more so than haloperidol are presented in rebuttal of contrary arguments presented by Singh and Kay (1978). The need for large numbers of subjects and multivariate statistics to assess between group differences on a large number of dependent variables and the problems associated with the use of correlated T-tests without correction of alpha level are discussed; and the position that psychiatric rating scales can have ordinal properties is defended. Singh and Kay's failure to find an antitherapeutic effect of anticholinergic drugs in chlorpromazine treated schizophrenics may stem from inadequate statistics, failure to use strictly double-blind raters, and concurrent staff problems that could have affected the patients' conditions. Numerous studies which have reported no change or worsening after stopping anticholinergic drugs and clinical improvement after adding anticholinergic drugs are reported. The recent report of increased brain choline acetyltransferase activity in schizophrenics is discussed in relation to the theory of a dopaminergic cholinergic imbalance in schizophrenia. 30 references. (Author abstract modified)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

003479 Alby, J.-M.; Ferreri, M. no address **/Clinical study of maprotiline in the treatment of depressive conditions in outpatient practice./** Etude clinique de la maprotiline utilisee en pratique ambulatoire dans le traitement des etats depressifs. Psychologie Medicale (Paris). 10(3):553-559, 1978.

Five physicians treating 50 depressed nonhospitalized patients responded to a questionnaire to determine the antidepressive activity and the side-effects of maprotiline when taken orally and prescribed by general practitioners. The results are presented in chart form and indicate age of the patients, type of depression, prescribed dosage and effectiveness. It is concluded that the antidepressive effectiveness and general lack of side-effects of maprotiline taken orally make it an effective medication for the treatment of moderate depression by the genera' practitioner. 33 references. (Journal abstract modified)

003480 Axelsson, Rolf; Martensson, Erik. Psychiatric Department III, Lillhagen's Hospital, University of Goteborg, S-422 03 Hisings Backa, Sweden **Relationship between serum concentrations of thioridazine and its main nonconjugated metabolites and the clinical response in thioridazine-treated patients.** Current Therapeutic Research. 24(2):232-242, 1978.

The relationship between clinical effect and serum concentration of thioridazine and its main nonconjugated metabolites was studied in a group of 38 thioridazine treated patients with acute paranoid psychosis. Patients were followed up for 3 to 5 weeks with determinations of their serum concentrations of total and unbound thioridazine, thioridazine side-chain sulfoxide, thioridazine side-chain sulfone, and thioridazine ring sulfoxide. The patients' clinical statuses were evaluated according to a comprehensive psychopathological rating scale. Within the serum concentration intervals (mean concentrations during the observation period) of either 0.70 to 1.70 microM/l total thioridazine or 1.3to 3.0microM/l unbound thioridazine or 14 to 30microM/l unbound thioridazine side-chain sulfoxide 13 out of 14 patients, 16 out of 17 patients and 18 out of 19 patients, respectively, responded with a reduction of their rating score of more than 50%. Above and below these limits only 12 out of 22 patients, 9 out of 19 patients, and 7 out of 17 patients, respectively, showed a reduction by more than 50%. It is suggested that there is a therapeutically optimal concentration interval for thioridazine corresponding to the observed concentration intervals. 9 references. (Author abstract modified)

003481 Ballenger, James C.; Post, Robert M. Section on Psychobiology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20014 **Therpeutic effects of carbamazepine in affective illness: a preliminary report.** Communications in Psychopharmacology. 2(2):159-175, 1978.

Preliminary results of double-blind placebo controlled trial with 10 manic-depressive patients are reported, in which seven patients improved on carbamazepine (Tegretol), an anticonvulsant used extensively in temporal lobe epilepsy and trigeminal neuralgia and which has been noted to have significant psychotropic effects in epileptics. Four patients had anitmanic or antipsychotic responses with exacerbations on carbamazepine withdrawal. In addition, one manic and two depressed patients improved on carbamazepine while three patients (two manic, one depressed) failed to respond. The potential mechanisms of psychotropic action of carbamazepine on norepinephrine neurotransmitter function or its effects as an anticonvulsant acting primarily in the limbic system are discussed. 71 references. (Author abstract modifed)

003482 Bhatia, Subhash C.; Varma, Vijoy K.; Amma, M. P. K. Dept. of Psychiatry, Creighton University School of Medicine.

Omaha, NE 68108 **A study of the relationship betwen urinary 5-hydroxyindoles and depressive states.** Indian Journal of Psychiatry (Lucknow). 20(1):6-14, 1978.

The urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA) was studied in 30 Ss: 10 normal controls, 120 patients with depressive neurosis, and 10 patients with manic-depressive psychosis, depressed type. Urinary 5-HIAA, a metabolic end product of serotonin was determined repeatedly for all Ss, both before and after treatment (either imipramine or electroconvulsive therapy). Results indicate significantly higher values in depressed patients, and these values decreased following successful treatment. There was a significant positive correlation between the severity of depression and the patient's urinary 5-HIAA values. 30 references. (Author abstract modified)

003483 Blackwell, Barry; Stefopoulos, Athanasios; Enders, Patrick; Kuzma, Ronald; Adolphe, Allen. Department of Psychiatry, Wright State University School of Medicine, Dayton, OH 45431 **Anticholinergic activity of two tricyclic antidepressants.** American Journal of Psychiatry. 135(6):722-724, 1978.

The peripheral anticholinergic and central nervous system effects of three dosage levels of two tricyclic antidepressants were investigated in a double blind study. Desipramine and amitriptyline were tested in nine adult female volunteers. It was found that five hours after administration, desipramine caused significantly less reduction in salivation, while amitriptyline produced more sedation and a greater number of subjective complaints. These results are consistent with anticholingergic profiles from animal experiments and suggest that clinically meaningful differences may exist among tricyclic antidepressants. 10 references. (Author abstract modified)

003484 Bowden, Charles L. 7703 Floyd Curl Drive, San Antonio, TX 78284 **Lithium-responsive depression.** Comprehensive Psychiatry. 19(3):227-231, 1978.

Problems in clarifying the types of depressive patients who respond positively to lithium carbonate therapy are reviewed, and clinical guidelines for recognizing likely lithium responsive depressive patients are presented. Diagnostic criteria and the limitations of nosologic systems with regard to depression are reviewed, and symptoms characterized by mild mood elevation, sequence of manic and depressive episodes, selective memory, and the interaction of personality with disease are discussed. Biologic and clinical characteristics of depressive patients who respond positively to lithium therapy are presented and theories of the mechanism of lithium's action are reviewed. 21 references.

003485 Bukreyev, V. I. Otdel psikhiatrii Khar'kovskogo nauchnoissledovatel'skogo instituta nevrologii i psikhiatrii, Kharkov, USSR /**The influence of pyridoxine on the psychopathology and pathochemistry of depressions of involutional age.**/ Vliyaniye piridoksina na psikhopatologiyu i patokhimiyu depressiy involyutsionnogo vozrasta. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 78(3):402-408, 1978.

The effect of pyridoxine (vitamin B6) on 48 patients with psychotic syndromes was investigated. Thirty-one Ss were diagnosed as involutional melancholics and 17, as manic-depressives. Ss ranged in age from 40 to 70, with the onset of illness coming after age 40 in all cases. Fourteen of the patients were suffering from their third attack of the disorder; 12 were suffering from their second. A control group of 17 age matched healthy persons was used for comparison. Pyridoxine treatment was found to have a positive therapeutic effect accompanied by an increase in noradrenaline excretion and a drop in relative adrenaline content. The obtained data support the significant role attributed to noradrenaline insufficiency in the pathogenesis of depressions. 10 references. (Journal abstract modified)

003486 Caroff, Stanley N. Department of Psychiatry, Montefiore Hospital, 111 E. 210th St., Bronx, NY 10467 **Klinefelter's syndrome and bipolar affective illness: a case report.** American Journal of Psychiatry. 135(6):748-749, 1978.

A case study illustrating an association between Klinefelter's syndrome and bipolar affective illness is presented. Klinefelter's syndrome is described as characterized by small, firm testes, azoospermia, gynecomastia, elevated urinary gonadotrophins, and a 47 XXY karyotype, and has been reported in association with a variety of psychiatric disorders, mental retardation, and criminality. It is suggested that the association of the syndrome with bipolar affective illness may be of significance in understanding the pathogenesis of affective disease. Possible causes of the association between the two conditions are discussed. 10 references.

003487 Chouinard, Guy; Young, Simon N.; Annable, Lawrence; Sourkes, Theodore L.; Kiriakos, Ramzi Z. Department of Psychiatry, McGill University, 1033 Pine Avenue West, Montreal H3A 1A1, Canada **Tryptophan-nicotinamide combination in the treatment of newly admitted depressed patients.** Communications in Psychopharmacology. 2(4):311-318, 1978.

At the 30th Annual Meeting of the American Psychiatric Association, New Research Programme, held in Toronto, Ontario, May 1977, which discusses the tryptophan - nicotinamide combination in the treatment of depressed patients. Eleven newly admitted depressed patients were given a combination of tryptophan and nicotinamide for 4 weeks. The initial daily dose of 2g tryptophan and 0.5g nicotinamide was gradually increased to 6g tryptophan and 1.5g nicotinamide. There was a significant improvement in the mean depressive symptomatology of the patients, as measured by the Hamilton and Beck Rating Scales, which was correlated with an increase in free plasma tryptophan. On the basis of percentage improvement on the Hamilton depression scales, there were three marked responders (50% improvement or more), four moderate responders (25-49%), and four nonresponders (less than 25%). Final free plasma tryptophan concentrations were correlated with their initial values, suggesting that patients who metabolize tryptophan slowly under normal conditions also tend to metabolize administered tryptophan slowly, resulting in higher plasma tryptophan levels and better therapeutic response. 3 references. (Author abstract modified)

003488 Coppen, A.; Ghose, K.; Montgomery, S.; Rama Rao, V. A.; Bailey, J.; Jorgensen, A. Medical Research Council Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **Continuation therapy with amitriptyline in depression.** British Journal of Psychiatry (London). 133(July):28-33, 1978.

Thirty two patients who had responded to amitriptyline (150mg daily) while suffering from a depression were allocated to either receive a placebo or remain on the same medication for a year. Plasma concentrations of the drug were regularly estimated. The results show that there was no correlation between plasma concentration and subsequent residual affective morbidity. Three of the patients did not take the prescribed amitriptyline despite encouragement and they all relapsed. Five of 16 patients who received placebos relapsed. None of the patients who continued to take the amitriptyline relapsed. It is emphasized that the patients studied were selected because they were apparent responders to amitriptyline. It is concluded that the patients should continue treatment with antidepressant medication for 8 months after apparent recovery, and care should be taken to

ensure patient's compliance. 16 references. (Author abstract modified)

003489 Coppen, Alec; Ghose, Karabi. Medical Research Council Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **Peripheral alpha-adrenoreceptor and central dopamine receptor activity in depressive patients.** Psychopharmacology (Berlin). 59(2):171-177, 1978.

The tyramine dose/pressor response test, the noradrenaline dose/pressor response test, and the phenylephrine dose/pressor response test were given to depressive patients before and after clinical recovery and to normal subjects. Depressive patients were more sensitive on all three tests than control subjects and tended to revert to normal after clinical recovery. Amitriptyline decreased the sensitivity to tyramine; this decrease was significantly correlated with the plasma concentration of nortriptyline, but drug-induced changes in the tyramine test did not correlate with clinical recovery. Patients became more sensitive to noradrenaline and less sensitive to phenylephrine while on amitriptyline; these changes were positively correlated with plasma levels of nortriptyline. Results of the bromocryptine/prolactin response test provided no evidence of altered dopamine receptor sensitivity in depressive patients. 17 references. (Author abstract modified)

003490 Cutler, Neal; Heiser, Jon F. University of California, Irvine, Medical Center, Orange, CA 92668 **Retrospective diagnosis of hypomania following successful treatment of episodic violence with lithium: a case report.** American Journal of Psychiatry. 135(6):753-754, 1978.

A case report describing the successful treatment of episodic violence with lithium is presented. The initial diagnosis was explosive personality, but upon the basis on further examinations and interviews a new diagnosis of hypomania was made. It is suggested that the difficulty in obtaining an accurate history may cause cases of primary affective disorder to be falsely diagnosed as emotional instability. A positive response to lithium therapy without side-effects is viewed as indicative of a diagnosis of affective disorder. 8 references.

003491 De Backer-Dierick, G.; Van Elsacker-Van Essche, M. Neuropsychiatric Hospital Reigerlo, B-8030 Beernem, Belgium **The use of penfluridol according to a new dosage regimen in the acute, stabilization and maintenance phases of psychosis.** Current Therapeutic Research. 24(2):193-203, 1978.

The efficacy of penfluridol as the sole therapy in the acute, stabilization, and maintenance phases of psychotic conditions, and in particular relapses of chronic schizophrenics, was evaluated in an open study incorporating a new treatment schedule. Twenty patients were evaluated by means of the Brief Psychiatric Rating Scale and the Discharge Readiness Scale on admission to the trial and at the end of each treatment phase. The need for neuroleptic co-medication, antiparkinsonian treatment, or hypnosedation was evaluated and is discussed. Of 18 patients who completed the study, 11 were ready for discharge within 1 to 3 months, three of them having received only penfluridol; the other eight occasionally needed adjunctive neuroleptic medication. Five additional patients were improved during the study, especially in activity or resocialization. In two other patients, no improvement was observed. It is suggested that a more flexible dosage schedule may improve the therapeutic results and reduce the need for additional medication. 3 references. (Author abstract)

003492 Donnelly, Edward F.; Waldman, Ivan N. NIMH, Saint Elizabeths Hospital, William A. White Building, Washington, DC 20032 **IQ as a predictor of antidepressant responses to lithium.** Psychological Reports. 42(3):898, 1978.

A sample of 30 females and 13 males hospitalized for depression were administered a median lithium dosage of 1500mg/day to investigate the potential value of IQ in predicting response to an antidepressant drug. Lithium and placebo were administered in identical capsules in a nonrandom design utilizing placebo and drug periods in each patient. Patients were rated twice daily on a 15 point scale. Results indicate that nonresponders to antidepressant drugs tend to have higher mean IQs than responders, but IQs are poor predictors of responsivity to these drugs. 4 references.

003493 Ghose, Karabi, Rama Rao, V. A.; Bailey, J.; Coppen, Alec. no address **Antidepressant activity and pharmacological interactions of ciclazindol.** Psychopharmacology (Berlin). 57(1):109-114, 1978.

The effectiveness of ciclazindol (CZD), a new tetracyclic compound, was investigated in 30 inpatients suffering from primary depressive illness. The therapeutic effect of CZD was similar to that of the established antidepressant amitriptyline, but significantly fewer subjective side-effects were reported. Patients treated with 100mg/day CZD showed decreased tyramine sensitivity, indicating that the drug has peripheral noradrenergic blocking activity, but no significant effect on postsynaptic alpha-receptors was observed. No correlation was observed between plasma levels of CZD and therapeutic outcome. 15 references.

003494 Goldman, Douglas. 179 East McMillan Street, Cincinnati, OH 45219 **Psychopharmacologic treatment of depression in private practice.** Psychiatric Journal of the University of Ottawa (Ottawa). 3(1):21-25, 1978.

A longitudinal, clinical assessment of depressive patients treated psychopharmacologically in private practice over a period of 20 years is presented. Data were obtained from the records of 837 patients whose depressions were subclassified into the following categories: 1) psychoneurotic depressions; 2) monopolar or chronic depressions; 3) bipolar mani-depressions; 4) depressions with somatic disorders (nontraumatic); 5) posttraumatic depressions 6) physical illness aggravated by depression; 7) situation reactions depressions; and 8) depressions with other psychotic reactions. The use and efficacy of pharmacotherapy are discussed. Data suggests that no specific medication is specific for any kind of depressive illness. Often patients who did not respond over a period of months to one medication improved when another was prescribed. It is concluded that all patients who could be properly classified showed some improvement, even if only moderate, under the influence of the mixed treatment of drugs plus psychotherapy. (Author abstract modified)

003495 Goodwin, Frederick K.; Muscettola, Giovanni; Gold, Philip W.; Wehr, Thomas. Laboratory of Clinical Science, NIMH, Bethesda, MD **Biochemical and pharmacological differentiation of affective disorders: an overview.** In: Akiskal, H., Psychiatric diagnosis. New York, SP Medical & Scientific Books, 1978. 493 p. (p. 313-336).

The potential and limitations of biological and pharmacological approaches to the broad problem of diagnosis and classification of affective disorders are examined. In particular, the question whether biological or pharmacological measures in their present state of development might help clarify the existing diagnostic confusion or might simply add to the confusion is addressed. These issues are developed by focusing on studies of biogenic amine metabolites in urine and cerebrospinal fluid. With the use of a three sphere model (biological findings, pharmacological response, and clinical history), some of the relationships reported in studies of affective illness are illustrated, and some pitfalls in the analysis of subgroups are explained. Preliminary findings from a relatively small number of patients are con-

sistent with animal studies on the differential effects of various tricyclic drugs on different amine neurotransmitter systems in the brain. 107 references.

003496 Gravem, A.; Engstrand, E.; Guleng, R. J. Department 1, Dikemark Hospital, N-1385 Solberg, Norway **Cis(Z)-clopenthixol and clopenthixol (Sordinol) in chronic psychotic patients: a double-blind clinical investigation.** Acta Psychiatrica Scandinavica (Kobenhavn). 58(5):384-388, 1978.

A comparison between the clinical effects of cis(Z)-clopenthixol and clopenthixol, which is a mixture of the pharmacologically active cis(Z)-isomer and the inactive trans(E)-isomer, is presented. A 2 month double blind trial was run using 57 psychotic patients. Ratings were recorded, evaluating severity of illness, therapeutic effect, possible interference of side effects with the patient's functioning, as well as any individual side effects, at months 0, 1, and 2. It is reported that the antipsychotic effect of cis(Z)-clopenthixol was equal to that of clopenthixol whereas the cis(Z)-isomer on a mg/mg basis was twice as active as clopenthixol. It is also reported that apart from the finding that the unspecific sedative effect appeared to be less marked with cis(Z)-clopenthixol, the type, degree, and frequency of side effects were the same in the two groups of patients. 5 references. (Author abstract modified)

003497 Green, Douglas O. 408 So. Center Medical Blvd., Portland, WA 99204 **Clinical importance of doxepin antidepressant plasma levels.** Journal of Clinical Psychiatry. 39(5):481-482, 1978.

The clinical significance of tricyclic antidepressant plasma levels is illustrated by a case study of the concomitants of doxepin plasma levels. Although still not widely available to the practicing psychiatrist, plasma levels can make an important difference in treating the drug resistant depressed patient. The concept of therapeutic plasma level range is discussed. 5 references. (Author abstract modified)

003498 Heefner, John D.; Wilder, Russell M.; Wilson, I. Dodd. Department of Medicine, Section of Psychological Medicine, Veterans Administration Hospital, Minneapolis, MN 55417 **Irritable colon and depression.** Psychosomatics. 19(9):540-543, 1978.

The relationship between irritable colon and depression was investigated through the use of self-rating symptom scales and the Zung Self-Rating Depression Scale. Thirty one subjects were followed for 2 months in a double-blind study employing desipramine hydrochloride (150mg/d) and an inactive placebo. Results demonstrated a correlation between the frequency of depression and patients with the syndrome. A clearly positive treatment effect with the placebo alone for both depressive symptoms and gastrointestinal complaints was also shown. It is suggested that tricyclic antidepressant therapy results in moderately greater improvement in symptoms than does treatment with placebo alone. Results should be considered tentative until following for a longer term is accomplished. 19 references. (Author abstract modified)

003499 Hendler, Nelson H. Department of Psychiatry, The Johns Hopkins Hospital, Osler 320, 601 North Broadway, Baltimore, MD 21205 **Spironolactone prophylaxis in manic-depressive disease.** Journal of Nervous and Mental Disease. 166(7):517-520, 1978.

In an attempt to define the role of aldosterone in manic-depressive disease spironolactone was given to six manic-depressive patients who had responded well to lithium, but had experienced a wide range of side-effects from lithium therapy. The effect which lithium therapy has on the central nervous system is compatible with all three theories regarding the basis of affective disorders: the biogenic amine theory, the electrolyte theory, and the membrane theory. Fluctuations in the hormone aldosterone during the various stages of manic-depressive disease could account for an etiological mechanism compatible with all three theories. Subjects were two male and four females ranging in age from 21 to 56 years old. On a minimum 1 year follow, five of the six patients were well maintained on this new drugup study regimen, further implicating aldosterone action in the etiology of manic-depressive disease. 31 references. (Author abstract modified)

003500 Hollister, Leo E. Veterans Administration Hospital, 3801 Miranda Ave., Palo Alto, CA 94304 **Treatment of depression with drugs.** Annals of Internal Medicine. 89(1):78-84, 1978.

Guidelines for the treatment of depression with drugs are presented. The classification, symptoms, and diagnosis of depression are described. Tricyclic antidepressants are cited as the drug of first choice for treatment, with monoamine oxidase inhibitors playing a secondary role. Differences in pharmacologic effects of tricyclics which might affect their use for individual patients are discussed. It is suggested that monitoring of plasma concentrations of tricyclics may reveal some sources of drug failure such as altered drug kinetics or noncompliance with treatment. The existance of numerous side-effects of antidepressant drugs is cited and attributed to extensions of known pharmacologic actions. The severe intoxication produced by overdoses is noted. 14 references. (Author abstract modified)

003501 Kampman, R.; Nummikko-Pelkonen, A.; Kuha, S. Muurolan sairaala SF-97145 Totonvaara, Finland **Tricyclic antidepressants in the treatment of depressions: a double-blind clinical comparison of clomipramine (Anafranil) and amitriptyline.** Acta Psychiatrica Scandinavica (Kobenhavn). 58(2):142-148, 1978.

The clinical efficacy of oral clomipramine (C) and amitriptyline (AMT) treatment (50-125mg/day) was compared over a period of 2 months in 72 depressive patients visiting a psychiatric outpatient clinic. Both drugs were equally effective as measured by the Hamilton Rating Scale for Depression. The two drugs were equipotent in relieving depressive symptoms and no statistically significant differences between the treatment groups were found. A trend in favor of C was seen in several parameters. The declines in the Hamilton Rating Scale scores and clinical evaluation scores were highly significant during the first 2 weeks of treatment in both groups. The most common unwanted effects were dryness of the mouth and fatigue. Side-effects were seen in 51% of the C group and 43% of the AMT group. The side-effects were generally mild and transient. 16 references. (Author abstract modified)

003502 Karlberg, Bengt E.; Kjellman, Bengt F.; Kagedal, Bertil Department of Internal Medicine, University Hospital, S-581 85 Linkoping, Sweden **Treatment of endogenous depression with oral thyrotropin-releasing hormone and amitriptyline.** Acta Psychiatrica Scandinavica (Kobenhavn). 58(5):389-400, 1978.

A comparison between the effects of thyrotropin releasing hormone (TRH) and amitriptyline on the symptoms of subjects with endogenous depression is presented. Six subjects received 80mg/daily of TRH and another six subjects received 100mg/daily of amitriptyline for 3 weeks in a double blind, randomized fashion. It is reported that the symptoms of four patients in the TRH treatment group, as measured by the Cronholm-Ottosson rating scale and global rating, showed improvements but not to the same degree as the group of patients given amitriptyline. Because of a significant negative correlation between free thyroxine index before treatment and therapeutic effect of TRH, it is concluded that there may be a subgroup of patients with endogenous depression with lower thyroid function who could benefit

from TRH administration. 44 references. (Author abstract modified)

003503 Kierkegaard-Hansen, A.; Pedersen, E. B.; Darling, S.; Amdisen, A. Psychopharmacology Research Unit, Aarhus University Department of Psychiatry, Psychiatric Hospital in Aarhus, DK-8240 Risskov, Denmark **Plasma renin concentration during lithium therapy.** International Pharmacopsychiatry (Basel). 13(3):133-137, 1978.

Two studies were undertaken to examine plasma renin concentration in manic-depressive patients during lithium therapy. In a longitudinal study, plasma renin concentration was determined in nine patients before the start of lithium treatment and at intervals during 3 months of treatment. In a transversal study, 18 patients on lithium for 2 to 20 years were compared with 11 controls. In the first study, plasma renin concentrations did not deviate significantly from pretreatment values during the treatment period. In the transversal study, no significant differences in plasma renin concentrations were found between experiments and controls nor were there any correlations between serum lithium and plasma renin concentrations. Results indicate that plasma renin concentrations remain unaffected by lithium administered in nontoxic doses. 7 references. (Author abstract)

003504 Kline, Nathan S. Rockland Research Institute, Orangeburg, NY 10962 **The perils of prescribing psychotropic drugs.** Resident & Staff Physician. 24(8):57-60, 1978.

Guidelines for the prescription of psychotropic drugs by psychiatrists are presented. Interactions between psychotropic drugs and other medications are described. The need to inform the patient's physician of psychotropic drug therapy in order to avoid confusion in the diagnosis of physical reactions is emphasized. Contraindications, side-effects, dosage levels, patient difficulties in comphrehending instructions, time needed for the drug to take effect, and diagnostic ambiguities are discussed as potential problem areas.

003505 Kripke, Daniel F.; Mullaney, Daniel J.; Atkinson, Martha; Wolf, Sanford. Veterans Administration Hospital (116), 3350 LaJolla Village Drive, San Diego, CA 92161 **Circadian rhythm disorders in manic-depressives.** Biological Psychiatry. 13(3):335-351, 1978.

Seven circular manic-depressives were studied through complete cycles of mania and depression to obtain longitudinal observations in rapidly cycling manic-depressives. The results show that in five subjects there was evidence that a circadian rhythm free ran fast and in five subjects there was evidence that lithium slowed a circadian rhythm. The palliative benefit of lithium may derive from slowing or delaying an overfast circadian clock to prevent desynchronization. Two subjects whose circadian clocks seemed too slow were lithium nonresponders. The conclusion is that since circadian clock frequency may be transmitted on an x-chromosome gene and may increase with age, a circadian etiology is consistent with the genetics and age distribution of manic-depressive illness. 59 references. (Author abstract)

003506 Lennox, I. G.: Asbury, J. F. P.; Couldrick, W. G. R.; Beswick, K. B. J. Didcot, Oxfordshire, England **Viloxazine and amitriptyline in depressive illness: a double blind controlled trial in general practice.** Practitioner (London). 220(1315):153-156, 1978.

A new antidepressant, viloxazine (Vivalan), chemically unrelated to the tricyclics, was compared in a controlled trial to the standard amitriptyline. Forty one patients whose affective disorder was marked by sustained depression of mood, loss of interest with inability to concentrate, and sleep and appetite disturbances entered the study. Nineteen received viloxazine and 22 amitriptyline and Hamilton ratings, global ratings, blood pressure and pulse rate, body weight change, and side-effects were studied. It is concluded that within the setting of general practice, viloxazine was equally effective as the standard amitriptyline, but had fewer side-effects and higher patient compliance. 15 references.

003507 Lesse, Stanley. 114 East 78th Street, New York, NY 10021 **Tranylcypromine (Parnate) -- a study of 1000 patients with severe agitated depressions.** American Journal of Psychotherapy. 32(2):220-242, 1978.

A study of 1000 patients with severe agitated depressions who were treated with tranylcypromine on an ambulatory basis during a period of 13 years is presented. It was administered in combination with tranquilizers, usually trifluoperazine. Tranylcypromine is a safe, rapidly acting, very effective antidepressant and appears to be the drug of choice in patients with agitated depressions. 33 references. (Author abstract)

003508 Liisberg, P.; Mose, H.; Amdisen, A.; Jorgensen, A.; Petersen, H. E. Hopfner Psychiatric University Clinic B, Psychiatric Hospital, DK - 8240 Risskov, Denmark **A clinical trial comparing sustained release amitriptyline (Saroten Retard) and conventional amitriptyline tablets (Saroten) in endogenously depressed patients with simultaneous determination of serum levels of amitriptyline and nortriptyline.** Acta Psychiatrica Scandinavica (Kobenhavn). 57(5):426-435, 1978.

The clinical effect of sustained release preparation of amitriptyline is comparied with that of conventional amitriptyline tablets in a double-blind crossover study with 24 patients suffering from endogenous depression. The sustained release preparation was given in a single evening dose of two thirds the total daily dose of conventional tablets (which was given three times a day). Serum concentrations of amitriptyline and its active metabolite, nortriptyline, were determined. No difference was found between the two preparations as regards either clinical effect or sideeffects It is concluded that no correlation could be shown between the clinical effects and the serum concentrations of amitriptyline and nortriptyline. 16 references. (Author abstract)

003509 Lipton, Morris A.; Carlsson, Arvid; Dunner, David L.; Goodwin, Frederick K.; Janowsky, David S.; Meltzer, Herbert Y.; Wyatt, Richard J. Biological Sciences Research of the Child Development Institute, University of North Carolina, Chapel Hill, NC 27514 **Biochemical and pharmacological predictors.** In: Akiskal, H., Psychiatric diagnosis. New York, SP Medical & Scientific Books, 1978. 493 p. (p. 337-362).

A selective overview of biochemical and pharmacological predictors in affective disorders is presented. Among other topics, the joint use of clinical, biochemical/pharmacological, and neurophysiological criteria is discussed. The potential use of lithium response and pharmacologically-induced hypomania as diagnostic indicators is evaluated. The issue of the ethics of drug trials also is considered.

003510 McCabe, Michael S.; Corry, Robert J. Dept. of Psychiatry, University of Iowa College of Medicine, Iowa City, IA 52242 **Psychiatric illness and human renal transplantation.** Journal of Clinical Psychiatry. 39(5):393-395, 398-400, 1978.

Physiological and psychological causes for psychiatric illness in renal transplant recipients were investigated. During an 18 month period 20 transplant recipients were evaluated in psychiatric consultation. A variety of psychiatric illnesses were noted with eight patients diagnosed with secondary depression according to psychiatric research criteria. Case histories of these patients indicate that corticosteroid and methyl-dopa therapy were

significant etiologic agents in the development of the depressive syndrome. Implications for the management of patients with depressed mood or slowed thinking are discussed. 29 references. (Author abstract)

003511 Mehta, Dinesh; Mehta, Shobhana; Mathew, Poyanil. Katherine Hamilton Mental Health Center, 620 Eighth Ave., Terre Haute, IN 47804 **Primary empty sella syndrome and bipolar affective illness: case report.** Journal of the American Geriatrics Society. 26(5):225-227, 1978.

A case hsitory of a 71-year-old woman who was transferred from a psychiatric hospital and then diagnosed with primary empty sella syndrome and bipolar affective illness is presented. The patient had a history of depression and hypomanic behavior. No endocrine, visual, or neurologic dysfunction was noted, however, the patient had received electroconvulsive therapy with no long-term adverse effects Remission of the affective illness has been maintained for 5 years with lithium carbonate therapy. It was found that: a) the empty sella syndrome is a nonprogressive condition; b) that electronconvulsive therapy is not a contraindication if the clinical state of the patient justifies it; c) the elderly patient with manic depressive illness of the bipolar type does just as well with lithium therapy as the younger patient. It is concluded that the age of the patient per se is not a contraindication for the use of lithium salts. 6 references. (Author abstract modified)

003512 Meyers, Barnett. 6 Algonquin Dr., Chappaqua, NY 10514 **Treatment of imipramine-resistant depression and lithium-refractory mania through drug interactions.** American Journal of Psychiatry. 135(11):1420-1421, 1978.

A case report of the treatment of imipramine resistant depression and lithium refractory mania through drug interactions is described. Normally therapeutic dosages of imipramine were supplemented with methylphenidate to raise blood levels of the antidepressant in a previously unresponsive patient, and chlorothiazide diuretics were added to lithium to reverse a nephrogenic diabetes insipidus (NDI) syndrome and to achieve satisfactory serum lithium levels. It has been estimated that approximately 70% of significant depressive episodes respond to supposedly adequate oral dosage of imipramine and that 80% of manic episodes respond to lithium. Idiosyncratic rapid metabolism of the tricyclic has been offered as an explantion for some impipramine treatment failures, while the development of an NDI syndrome may explain many lithium failures. 10 references.

003513 Morozov, G. V.; Lukacher, G. Ya.; Anokhina, I. P.; Kudryavtsev, I. A.; Morozova, T. G.; Kogan, B. M. Tsentral'nyy nauchno-issledovatel'skiy institut sudebnoy psikhiatrii imeni V. P. Serbskogo, Moscow, USSR **/L-dopa treatment of reactive stuporous states./** Lecheniye reaktivnykh stuporoznykh sostoyaniy preparatom L-dofa. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 78(4):537-543, 1978.

Thirty male patients with stuporous conditions arising from mentally traumatic situations were treated with L-dopa. The mental state of 25 of the patients was diagnosed as psychogenic; the other 5 were schizophrenics. All the patients except two were over 20 years old. The 25 patients with the reactive syndrome were assumed to be curable by means of L-dopa because of the similarity of a number of their clinical and biochemical manifestations with those of an akinetic rigidity of Parkinson's disease where the drug has proven very effective. Seven of the 25 recovered after treatment with L-dopa, three showed significant improvement, five showed some improvement, and 10 showed no improvement. The drug was most effective against psychomotor inhibition in Ss with a monomorphically structured syndrome. The use of L-dopa with the five schizophrenic patients was ineffective. 12 references. (Journal abstract modified)

003514 Murphy, J. Eric; Bridgman, K. M. no address **A comparative clinical trial of mianserin (Norval) and amitriptyline in the treatment of depression in general practice.** Journal of International Medical Research (Northhampton). 6(3):199-206, 1978.

A double-blind controlled comparative trial of mianserin (Norval) and amitriptyline was conducted in general practice. Fifty-one patients were treated with amitriptyline and 55 with mianserin. The dosage for the first week was 25mg three times daily (t.d.s.)for amitriptyline and 10mg t.d.s. for mianserin, increasing to 50mg t.d.s. and 20mg t.d.s. respectively for the subsequent three weeks. Both drugs proved equally effective in relieving th symptoms of primary depression but mianserin showed a reduced incidence of side-effects which was statistically significant. 11 references. (Author abstract)

003515 Nuller, Yu. L.; Ostroumova, M. N. Leningradskiy nauchno-issledovatel'skiy psikhonevrologicheskiy institut im. V. M. Bekhtereva, Leningrad, USSR **/Disturbance of homeostatic regulation of adrenal function in patients with endogenous depression./** Narusheniye gomeostaticheskoy regulyatsii funktsii nadpochechnikov u bol'nykh endogennoy depressiyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakov (Moskva). 78(3):381-385, 1978.

Twenty two patients with endogenous depressions (age range 18 to 65) were treated with dexamethasone. Nineteen were diagnosed as manic-depressives, while 3 had involutional depressions. Six of the patients suffered from classical melancholy, 13 were paranoid, and the remaining 3 had depersonalization syndromes. Sensitivity to the beneficial inhibitory action of the drug was determined by a drop in 11-oxycorticosteroids in the blood content. In 20 of the patients the dexamethasone test was unsatisfactory during the depression's peak period, but 14 of them were more receptive to the drug's action during nonpeak periods. It is concluded that insufficient regulation of glucocorticosteroids in the blood is a significant link in the pathogenesis of endogenous depressions due to disorders of metabolism of the cerebral biogenic amines. 26 references. (Journal abstract modified)

003516 Potter, William Z.; Zavadil, Anthony P., III; Goodwin, Frederick K. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Prediction of steady-state plasma concentration of imipramine.** Bethesda, MD, NIMH, 1978. 21p.

Biological aspects of affective illness were investigated by studying concentrations of imipramine and its metabolite desipramine assay. Six female patients in a psychiatric ward with diagnoses of major affective disorders were administered 1.5mg/kg of imipramine. Blood samples were drawn at 2 hour or longer intervals for up to 2 hours and were subjected to a very sensitive and specific gas chromatographic mass spectrometric assay. A high correlation between steady state plasma and cerebrospinal fluid concentrations was demonstrated. It is concluded that a clinically useful prediction of ultimate steady state concentrations of imipramine is feasible at the outset of treatment. 22 references.

003517 Rhead, John C. Taylor Manor Hospital, Ellicott City, MD 21043 **The implications of psychedelic drug research for integration and sealing over as recovery styles from acute psychosis.** Journal of Psychedelic Drugs. 10(1):57-64, 1978.

Research is cited on the use of psychedelic drugs, such as LSD, as adjuncts to psychotherapy to explain styles of response

from acute psychosis. Response styles range from integration to sealing over. It is noted that individuals who successfully seal over are reluctant to discuss the thoughts and feelings they experienced while actively psychotic, often lack awareness of the details of their psychotic episode, and fail to place their psychotic experiences into a personal context. Integration describes a process by which a continuity is recognized between thoughts and feelings experienced during psychosis and prepsychotic and postpsychotic mental life. Some theoretical aspects of sealing over apply to treatment failures of psychedelic drug assisted psychotherapy as well as to experiences from casual drugtaking. The theory and techniques of psychedelic drug assisted psychotherapy are summarized in relation to the standpoint in libido economy and a structural approach to the formation of psychotic symptomatology. Implications for the treatment of schizophrenics by psychedelic drug assisted psychotherapy are discussed. 27 references.

003518 Rybakowski, Janusz; Frazer, Alan; Mendels, Joseph. Dept. of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, PA 19104 **Lithium efflux from erythrocytes incubated in vitro during lithium carbonate administration.** Communications in Psychopharmacology. 2(2):105-112, 1978.

To investigate the effect of the administration of lithium carbonate on the activity of the lithium-sodium countertransport system, the efflux of the lithium ion from erythrocytes into medium containing the cation was measured in control subjects and patients with affective disorders both prior to and during the administration of lithium carbonate. Administration of lithium carbonate produced a significant rise in the lithium ratio measured in vitro, which suggests that lithium-sodium counterflow activity was inhibited, an effect which was apparent as early as 3 days after administration of lithium carbonate and persisted for at least 7 days after discontinuation of lithium carbonate, with pretreatment values of the lithium ratio being reached 14 days after the drug was stopped. It remains to be determined whether this pharmacological effect of the lithium ion is related to its clinical actions. 20 references. (Author abstract modified)

003519 Rybakowski, Janusz; Frazer, Alan; Mendels, Joseph; Ramsey, T. Alan. Dept. of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, PA 19104 **Erythrocyte accumulation of the lithium ion in control subjects and patients with primary affective disorder.** Communications in Psychopharmacology. 2(2):99-104, 1978.

To investigate the role of erythrocyte accumulation of the lithium ion in patients with primary affective disorder, the accumulation of the lithium ion by erythrocytes relative to the plasma concentration of the cation (the lithium ratio) was measured both in control subjects and in patients with either unipolar of bipolar affective disorders. In the control subjects, the lithium ratio was measured in two different ways: 1) 21 subjects took lithium carbonate for 3 weeks and the lithium ratio was measured in vivo; and 2) in 28 subjects, the lithium ratios was measured in vitro. All patients received lithium carbonate and had their lithium ratios measured in vivo. As a group, bipolar patients had a mean lithium ratio that was significantly higher than that measured in the control population; unipolar patients did not. This significant difference was seen with either male or female patients. 15 references. (Author abstract)

003520 Salzman, Carl; Shader, Richard I. Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Depression in the elderly. II. Possible drug etiologies; differential diagnostic criteria.** Journal of the American Geriatrics Society. 26(7):303-308, 1978.

Drugs which may contribute to depression in the elderly are reviewed, and criteria for the diagnosis of depression in the elderly are presented. Drugs used in the treatment of a medical disease which may cause depression include digitalis, antihypertensive agents, and antiparkinsonism drugs. Psychotropic drugs which may cause depression are neuroleptic drugs and antianxiety drugs. Polypharmacy, leading to drug interactions, is common in prescribing for the elderly. Although depression is not commonly associated with drug interactions, other mental effects such as confusion, delirium, and psychosis can occur as a result of interaction between medical drugs, or between medical and psychiatric drugs. Signs and symptoms of depression are discussed, and some of the nonpsychologic states that should be considered are summarized. Because of the interweaving of depression, physical and drug effects, every psychiatric evaluation of the depressed elderly patient should include the following: a careful physical examination and noninvasive laboratory tests, a detailed appraisal of the medical and over-the-counter drugs taken by the patient, and psychiatric interviews with indirect and nonthreatening questions. 52 references.

003521 Sim, Myre; Gordon, E.B.; Nicol, C.G. Department of Psychiatry, University of Ottawa, Ottawa, Canada **Oxypertine in combination with imipramine: a controlled trial.** The Journal of International Medical Research (Northampton). 6(1):4-10, 1978.

A method for the controlled assessment of two agents for possible interaction in the treatment of endogenous depression is described. The experiment consisted of dose ranging the supplementary agent (oxpertine 30mg and 60mg daily or matching placebo) during week 2 to week 6, having established all subjects on a therapeutic dose of imipramine during week 1. Subjects were adults of either sex suffering from psychotic (endogenous) depression with a total score on the Hamilton Depression Scale of 20 or more and who were hospital inpatients. The trial did not show any advantage in combining oxypertine with imipramine. However, the findings suggest that it is possible to design a trial where two active agents with a hypothetical synergistic effect can be combined and their function reliably assessed under controlled conditions. 6 references. (Author abstract modified)

003522 Sorensen, Birgitte; Kragh-Sorensen, Per; Larsen, Niels-Erik; Hvidberg, Eigill F. Department of Psychiatry, Bispebjerg Hospital, Copenhagen, Denmark **The practical significance of nortriptyline plasma control. A prospective evaluation under routine conditions in endogenous depression.** Psychopharmacology (Berlin). 59(1):35-39, 1978.

The practice of monitoring plasma levels of tricyclic antidepressants during routine treatment of endogenously depressed patients was evaluated. Nortriptyline (NT) plasma levels were measured in 34 patients during the second week of NT treatment, and dosages were adjusted if plasma levels were outside the recommended therapeutic range of 50-150ng/ml. A cautious dose policy led to low plasma levels, followed by dose increase in about 40% of the patients. Plasma level exceeded in the upper limit only in a few patients. Results indicate that controlling the NT plasma concentration may offer a therapeutic advantage. 14 references. (Author abstract modified)

003523 Sugerman, A. Arthur. Carrier Clinic Foundation, Belle Mead, NJ **A controlled trial of a new antidepressant, WIN 27147-2.** Current Therapeutic Research. 24(2):227-231, 1978.

A controlled trial of WIN-27147-2, a new antidepressant, is discussed. In a double-blind study, WIN-27147-2 was given to 13 and imipramine to 7 acutely depressed patients for periods of 2 to 6 weeks after a 5 to 7 day baseline placebo period. Maximum daily doses were 300mg of imipramine and 600mg of

WIN-27147-2. Antidepressant activity of the two drugs appeared comparable with some differences in side-effects; the investigational compound appeared more sedative and less anticholinergic. The drug has been withdrawn from testing because of later evidence of significant toxicity. 2 references. (Author abstract)

003524 Sullivan, John L.; Zung, William W. K.; Stanfield, Charles N.; Cavenar, Jesse O., Jr. Psychiatry Service, Veterans Administration Hospital, 508 Fulton Street, Durham, NC 27705 **Clinical correlates of tricyclic antidepressant-mediated inhibition of platelet monoamine oxidase.** Biological Psychiatry. 13(3):399-407, 1978.

The relationship between tricyclic mediated inhibition of platelet monoamine oxidase (MAO) and resolution of clinical signs and symptoms which are commonly associated with the depressive syndrome, were examined. The results indicate the sedative hypnotic effects of the tricyclics closely correlate with the magnitude of platelet MAO inhibition. It appears that these effects may be mediated through alterations in the metabolism of serotonin and/or the phenylethylamines. 21 references. (Author abstract)

003525 Talley, Joseph H. no address **When antidepressants don't work.** Clinical Medicine. 85(5):11-17, 1978.

Pitfalls that can result in treatment failure with tricyclic antidepressants are discussed as well as means of circumventing these pitfalls. A major reason for treatment failure is diagnostic error and confusion between chronic neurosis and true endogenous depression. Other reasons for failure include inappropriate selection of a specific tricyclic drug, inappropriate dosage, and inadequate length of therapy. Often the patient does not comply with the treatment schedule because the physician has not adequately discussed the drug regime, toxicity, possible side-effects, and addiction potential of the tricyclic antidepressants. Failure on the part of the physician to convince the patient that he is suffering from a real disease requiring treatment could also reduce the effectiveness of the therapy. 4 references.

003526 Tobin, Joseph M.; Robinson, Geraldine M. Helwig; Bindelglas, Paul M.; Crupie, Joseph E.; Dee, George. Northwest Psychiatric Clinic Research Center, Eau Claire, WI **Comparable efficacy of imipramine HCL and imipramine pamaote: a pooled statistical report.** Psychiatric Journal of the University of Ottawa (Ottawa). 3(1):33-38, 1978.

Imipramine HC1 and imipramine pamoate in comparable doses were compared with respect to efficacy and safety using a double blind procedure that was administered by common protocol at three separate centers to depressed patients. Results indicate that the single dose, long lasting imipramine pamoate, administered an hour before bedtime, was not statistically less effective than imipramine HC1 administered on a t.i.d. regime. Results of both drugs indicate statistical significance in improvement between baseline and the final visit. The onset of therapeutic effect was comparable for both forms of imipramine. There were no significant differences in treatment emergent signs and symptoms or other side-effects attributable to the drug. 9 references. (Author abstract modified)

003527 Tsutsui, Sueharu; Namba, Tsunehiko; Hashimoto, Shinichi; Yamazaki, Hiroki. Second Dept. of Internal Medicine, Toho University School of Medicine, Omori-Nishi 6-11-1, Ota-ku Tokyo, 143 Japan **A case of depression showing improvement in TRH test by combined treatment by dimetacrine tartrate and thyroid hormone.** Japanese Journal of Psychosomatic Medicine (Fukuoka). 18(4):321-326, 1978.

A 45-year-old male was treated with triiodothyronine (T3) in combination with dimetacrine tartrate for his sustained depressive state due to a traffic accident. Low TSH response to TRH test was found without abnormalities of thyroidal functions. The patient quickly responded to the combined treatment, and his psychosomatic improvement was paralled by the improvement of TSH response. A literature study of the TRH test and of combined treatment for depression by T3 and antidepressants was also made and discussed. 28 references. (Journal abstract modified)

003528 Vinar, O.; Vinarova, E. K ovcinu 1519, 182 00 Prague 8, Kobylisy, Czechoslovakia **Lithium dosage and age of patients.** Activitas Nervosa Superior (Praha). 20(1):91-92, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the relationship between lithium dosage, lithium blood level, and age of patients is described. A sample of 32 patients was given lithium for prophylaxis of relapses of manic-depressive psychosis, and the relationship between dosage, blood level and age was measured. Results indicate that younger patients need more lithium tablets to reach blood levels which have prophylactic effects. 3 references.

003529 Wald, David; Ebstein, Richard P.; Belmaker, Robert H. no address **Haloperidol and lithium blocking of the mood response to intravenous methylphenidate.** Psychopharmacology (Berlin). 57(1):83-87, 1978.

Ten euthymic manic-depressive patients with therapeutic plasma lithium levels were each given two intravenous (i.v.)infusions of 30mg methylphenidate. The infusions were separated by at least 3 days; before one infusion each patient was given 5mg haloperidol i.v. and before the other each was given an identical volume of saline. Saline pretreated patients showed marked activation and euphoriant responses despite therapeutic lithium levels. Haloperidol pretreatment reduced this response in three patients and eliminated the euphoriant and activating response in the remaining seven. Results are consistent with the existence of a dopaminergic step in the induction of methylphenidate induced activation and euphoria. 25 references. (Author abstract modified)

003530 Wald, David; Lerner, Jacob. Department of Psychiatry, Eitanim Government Hospital, Mobile Post Shimshon, Israel **Lithium in the treatment of periodic catatonia: a case report.** American Journal of Psychiatry. 135(6):751-752, 1978.

A case report describing the use of lithium in the treatment of periodic catatonia is presented. During 8 months hospitalization, a 44-year-old woman received high doses of neuroleptic drugs with no effect on her clinical state. After only one week of lithium carbonate treatment, the patient became symptom free for 4 months until discharge. It is suggested that the effectiveness of lithium can be attributed to the existence of similarities between periodic catatonia and bipolar affective disorders. 10 references.

003531 Whitlock, F. A.; Evans, L. E. J. Department of Psychiatry, Clinical Sciences Building, Royal Brisbane Hospital, Brisbane 4029, Australia **Drugs and depression.** Current Therapeutics (Seaforth, Australia). 19(4):97-100, 103, 105, 109-110, 113-114, 116-117, 119-120, 123-124, 1978.

Studies of the relationship between drugs and depression are reviewed. An analysis of the biochemical aspects of depression indicates that any drug depleting the levels of dopamine, noradrenaline and 5-hydroxytryptamine (5-HT), or drugs that augment the levels and availability of acetylcholine in the brain, and drugs potentiating the activity of monoamine oxidase may in certain circumstances cause depression. Drug-induced depres-

sion is most likely to occur in individuals genetically predisposed to depression or who have had a previous depressive illness. Only a relatively small number of drugs precipitate depressive symptoms with any frequency. Drugs most commonly implicated are long-acting antipsychotics, barbiturates, ethanol, oral contraceptives and antihypertensive agents. Some drugs (reserpine) cause depression as a side-effect, whereas others (fenfluramine) cause depression when withdrawn too rapidly. It is concluded that a distinction must be made between changes which occur during drug treatment and the patient's reaction to the disease being treated. (Author abstract modified)

003532 Wood, K.; Coppen, A. Medical Research Council Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey KT19 8PB, England **The effect of clofibrate on total and free plasma tryptophan in depressed patients.** Neuropharmacology (Oxford). 17(6):428-430, 1978.

The effects of clofibrate, which displaces tryptophan from its plasma protein binding sites, were examined in depressed patients and control Ss. Baseline plasma free tryptophan levels were significantly different in control Ss and depressed patients. The level of total tryptophan was significantly reduced in both groups after treatment with clofibrate for 3 days, but only the depressed patients had significantly elevated free plasma tryptophan concentrations relative to their baseline values. The concentration of plasma proteins could not account for this difference in tryptophan binding. The concentration of nonesterified fatty acids (NEFA) was significantly lower in the plasma of controls than in the patients' plasma, but no correlation could be found between free plasma tryptophan levels and NEFA levels. The differential effect of clofibrate on plasma tryptophan in controls and depressed patients may be the result of reduced uptake of tryptophan by the tissues in depressed patients. 10 references.

003533 Zvolsky, P.; Majsky, A.; Dvorakova, M.; Soucek, K.; Zemek, P.; Vinarova, E. Psychiatric Research Unit of Charles University, ke Karlovull, 12821 Prague, Czechoslovakia **Histocompatibility antigens in lithium treated manic-depressive patients.** Activitas Nervosa Superior (Praha). 20(1):72, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, histocompatibility antigens in lithium treated manic-depressives patients are discussed. The incidence of HLA-A and B antigens was determined in two groups of manic-depressive patients, mostly bipolar, prophylactically treated with lithium carbonicum. A significantly increased incidence of HLA-B7 antigen was found in the group composed of 14 patients with relatives suffering from manic-depressive psychosis or schizophrenia compared to a group without any psychiatric disorder among their relatives. 2 references.

10 DRUG TRIALS IN NEUROSES

003534 Bant, Wendy P. Middlewood Hospital, Sheffield, England **Antihypertensive drugs and depression: a reappraisal.** Psychological Medicine (London). 8(2):275-283, 1978.

The relationship between antihypertensive drugs and depression was investigated in 89 hypertensive outpatients and 46 nonhypertensive chronically physically ill outpatients over a 1 year period. Each patient completed the British Hospital Progress Test, a self-rating mood scale, at his first clinic attendance, and eight subsequent questionnaires were sent throughout the year. The results show a high prevalence of depression in both groups of patients. Hypertensive patients with psychiatric histories had a higher prevalence of depression than the comparison patients, which was accounted for by a significant number of depressions occurring in methyl dopa treated patients with psychiatric histories. The high number of noncompleters was expected due to the stringent criteria of voluntarily completing eight questionnaires. 16 references. (Author abstract modified)

003535 Bowden, Charles L. 7703 Floyd Curl Drive, San Antonio, TX 78284 **Double-blind placebo-controlled trial of ketazolam in anxiety.** Current Therapeutic Research. 24(2):170-178, 1978.

Ketazolam, a new, long-acting benzodiazepine, was compared to placebo in a 4 week double-blind study in 77 psychiatric outpatients with moderate to severe anxiety. The average optimum dose of ketazolam was 58.6mg (range, 25 to 125 mg) given in a single bedtime dose. Fifteen patients in the placebo group (41%) dropped out of the study; 12 because of ineffectiveness of the medication and 3 because of intolerable side-effects. In the ketazolan group, 5 patients (13%) dropped out because of ineffectiveness of the medication. This difference between treatment groups was statistically significant. Ketazolam was significantly more effective than placebo in reducing symptomatology on 10 of 14 Hamilton Anxiety Rating Scale categories and total scores, the Physician's and Patient's Global Impressions, and the Patient's Self-Rating Symptom Scales. The average number of side-effects per patient receiving ketazolam was less at every evaluation period than for patients receiving placebo. 8 references. (Author abstract)

003536 Celani, T.; Iorio, G.; Vacca, L.; Amati, A.; Del Vecchio, M. Department of Psychiatry, University of Naples, 1st School of Medicine, Naples, Italy **Electroencephalographic control with frequency analysis in depressed patients treated with SAMe.** Current Therapeutic Research. 23(4):525-527, 1978.

The effect of the antidepressant S-adenosyl-L-methionine on cerebral activity was investigated. Eighteen depressed patients treated with the drug submitted to electroencephalographic examination before and during treatment. A statistical comparative analysis showed no significant effects. It is concluded that S-adenosyl-L-methionine is an effective antidepressant which does not interfere with bioelectrical cerebral activity. 3 references. (Author abstract modified)

003537 Donald, J. F.; Molla, A. Layes. no address **A controlled study comparing a three times daily dose of chlordiazepoxide with a single night-time dose of trancopal in the control of zixiety, using a double-blind, double-dummy technique.** Journal of International Medical Research (Northampton). 6(2):105-110, 1978.

A double-blind, double dummy between patient study in general practice was carried out to compare the effectiveness of a single, night time dosage of Trancopal at night and a chlordiazepoxide placebo capsule three times daily or 10 mg of chlordiazepoxide three times daily and one or two Trancopal placebo tablets at night. Three assessments were made using a physicians' rating scale (modified Hamilton Scale). Results indicate that each treatment group improved considerably over the period of the study both for sleep and anxiety ratings. A statistically significant correlation was found between improvement in day time fatigue and loss of energy and improvement in sleep disturbance only in the Trancopal group. Loss of concentration was analyzed separately in patients over 40-years-old and there was a significant improvement in the physicians' rating in the Trancopal group. There was a very close correlation throughout between the physician's and patient's own assessment of improvement. Few side-effects not already reported at the start of the trial were reported on either treatment. It was concluded that Trancopal at a usual dosate of 400mg at night offers an effective alternative to a divided dose of chlordiazepoxide. 4 references. (Author abstract modified)

003538 Fabre, Louis F.; McLendon, David M.; Stark, Paul. Fabre Clinic, 5503 Crawford St., Houston, TX 77004 **Nabilone,**

a cannabinoid, in the treatment of anxiety: an open-label and double-blind study. Current Therapeutic Research. 24(2):161-169, 1978.

The use of nabilone, a cannabinoid, in the treatment of anxiety is evaluated. Nabilone was found to be significantly superior to placebo in the treatment of anxiety, and was found to improve the psychic and somatic concomitants of anxiety as well as feelings of depression. The drug proved to be fast acting, with dramatic reductions in anxiety on the first day of evaluation. Three milligrams of nabilone a day prove to be an effective dosage. Bothersome side-effects did develop, especially dry mouth; however no serious side-effects were detected and patients did not experience euphoria as would be expected with marihuana-like compounds. Nabilone did not result in any noteable changes in laboratory values, except for an insignificant reduction in blood pressure. 9 references. (Author abstract modified)

003539 Gomez-Lozano, Pedro. San Ignacio University Hospital (Javeriana) Medical School, Bogota, Columbia **Management of acute anxiety syndrome with parenterally administered lorazepam.** Journal of International Medical Research (Northampton). 6(3):186-192, 1978.

After the preliminary successful use of injectable lorazepam in calming 20 patients who presented with acute anxiety crises, a formal study of 115 other such patients was carried out. All were seen either in a hospital emergency room or on an emergency outpatient basis in private practice. Treatment consisted of an initial intravenous injection of lorazepam (3mg) followed, if necessary, by up to three further injections within a 24 hour period. The result was usually dramatic: complete abolition or reasonable control of symptoms within 30 minutes in all but two patients. The major effect was relaxant and sedative; 62 patients slept following the injections, although 55 could be easily aroused, 7 could not. Of the other patients, 49 remained awake but relaxed; only 4 remained tense and were regarded as treatment failures. No significant side-effects or changes in vital signs were noted. The results support and extend those reported by other investigators in a recent controlled, double-blind (but otherwise similarly conducted) trial. 5 references. (Author abstract)

003540 Lal, Narottam; Sharma, Mukul. Dept. of Psychiatry, K. G.'s Medical College, Lucknow, India **Role of narcosuggestions in hysteria.** Indian Journal of Psychiatry (Lucknow). 20(1):71-75, 1978.

The utility of chemical narcotherapy in treating 189 individuals with conversion hysteria is evaluated. Following thiopentone sodium administration, it was impressed upon the patient during narcosuggestion sessions that they would get rid of their symptoms as a result of treatment and injections. It was observed that: 1) the majority of patients responded favorably to the procedure; 2) cases with acute onset, and those seen at an earlier stage showed much better response; and 3) those with precipitating events recovered promptly. 9 references.

003541 Lapierre, Y. D. Department of Psychiatry, Ottawa General Hospital, 197 Cumberland, Ottawa, Ontario, Canada **Effectiveness of SCH 12679, a benzazepine, in the treatment of anxiety neurosis.** Current Therapeutic Research. 24(2):204-208, 1978.

The effectiveness of SCH-12679, a new benzodiazepine, in the treatment of anxiety neurosis was studied in 10 patients. One patient was dropped from the study after an adverse reaction following the first dose (25mg) of the drug. Another was withdrawn after a suicide attempt on the sixth day of treatment and one elected to drop out on the twelfth day because she had failed to respond. Of the remaining 7 patients, 4 were markedly improved, 2 moderately and one minimally after 4 weeks of treatment. 5 references. (Author abstract)

003542 Lapierre, Y. D.; Oyewumi, L. K.; Ghadirian, A.; Butter, H. J. Psychopharmacology Unit, Ottawa General Hospital, 197 Cumberland, Ottawa, Ontario, K1N 7H4, Canada **A placebo-controlled study of bromazepam and diazepam in anxiety neurosis.** Current Therapeutic Research. 23(4, Section 2):475-484, 1978.

Bromazepam, a new benzodiazepine, was compared with diazepam in a double-blind, placebo controlled study. Forty five outpatients with prolonged anxiety symptoms were treated with equimolecular doses of bromazepam and diazepam for 2 weeks. Bromazepam was found to be superior to diazepam in these patients and there was evidence to suggest the superiority of bromazepam over diazepam and placebo in the psychic anxiety and somatic anxiety clusters of the Hamilton Anxiety Rating Scale. Though diazepam increased the patients' ego on testing, bromazepam decreased their feelings of insecurity and tension. The results cast doubt on the sensitivity of the Zung Self-Rating Anxiety Scale and the validity of its cutoff score of 45. Equal numbers of patients reported the side-effects of drowsiness. One patient on bromazepam developed a toxic confusional state and had to be withdrawn from the study. Further studies of longer duration are suggested to clarify this side-effect. 15 references. (Author abstract)

003543 Pinta, Emil R. Dept. of Psychiatry, Ohio State University, Columbus, OH 43210 **Treatment of obsessive homosexual pedophilic fantasies with medroxyprogesterone acetate.** Biological Psychiatry. 13(3):369-373, 1978.

The treatment of a male patient with obsessive homosexual pedophilic fantasies, with psychotherapy and medroxyprogesterone acetate (MPA), a progestin with antiandrogen activity, is discussed. Long acting MPA was administered for a 2 month period and caused a prompt and drastic reduction in fantasies and in the anxiety and depression generated by them. The findings show MPA has psychological benefits that outlived its physiologic activity. 20 references. (Author abstract)

003544 Rickels, Karl; Weise, Charles C.; Feldman, Harold; Fee, Eugene A.; Wiswesser, George. Psychopharmacology Research and Treatment Unit, Department of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104 **Loxapine in neurotic anxiety: some modifiers of treatment response.** Journal of International Medical Research (Northampton). 6(3):180-185, 1978.

The anxiolytic properties of chlordiazepoxide, loxapine, and a placebo were compared with 135 anxious neurotic outpatients in a double-blind trial of 6 weeks duration. Two subgroups of anxious neurotic outpatients, those with high depressive secondary symptoms and those with high schizoid tendencies, improved more with loxapine than with placebo. Chlordiazepoxide was very little affected by initial level of either depression or schizoid symptoms, and, even in patients high in these symptom dimensions, loxapine did not only not surpass chlodiazepoxide but frequently was slightly less marked in its antianxiety properties. It is concluded that an indication for loxapine may exist only in those anxious patients high in secondary depression or schizoid tendencies who have failed to respond to an appropriate course of anxiolytic therapy with benzodiazepines. 9 references.

003545 Robinson, Donald S.; Nies, Alexander. Department of Pharmacology, Marshall University School of Medicine, Huntington, WV 25701 **Antidepressant drug levels and clinical response.** Lancet (London). 2(8080):100, 1978.

A letter to the editor addresses the problem of research studies which fail to find a clinically useful relationship between

plasma tricyclic antidepressant (TCA) levels and therapeutic effects. It is reported that a study of 49 amitriptyline treated (150mg/day for 6 weeks) outpatients resulted in the following: although 65% of the patients showed improvement, no significant relationship of plasma amitriptyline, nortriptyline, or combined TCA levels to patient response was found. This is in general agreement with the report of the World Health Organization collaborative study which failed to find a significant relationship between plasma TCA levels and clinical effects in amitriptyline treated patients. Most of the studies reporting positive findings have had very small samples, it is claimed, and thus suffer statistical limitations. 3 references.

003546 Simon, P.; Lecrubier, Y.; Jouvent, R.; Puech, A. J.; Allilaire, J. F.; Widlocher, D. Departement de Pharmacologie, Faculte de Medecine Pitie-Salpetriere, 91, Boulevard de l'Hopital, F-75634 Paris Cedex 13, France **Experimental and clinical evidence of the antidepressant effect of a beta-adrenergic stimulant.** Psychological Medicine (London). 8(2):335-338, 1978.

In an uncontrolled pilot study, a group of 49 patients with depressive illnesses were treated intravenously with salbutamol, a beta-adrenergic stimulant, to estimate its therapeutic efficacy upon depression. The patients were classified into four types of depression: 1) bipolar endogenous, 2) monopolar endogenous, 3) severe depressive reactions, and 4) less severe depressive reactions. Treatment lasted from 6 to 10 days, with the daily dose progressively increased from 3 to 6mg. Between the third and fifth day, improvement was general among all patients and affected the whole depressive syndrome (mood, psychomotor retardation, suicidal ideas, and anxiety). A markedly disinhibitory effect was noted in all patients, which might have been related to the rapid disappearance of anxiety. Adverse side-effects (such as tachycardia) were minimal and disappeared when the infusions were stopped. Results indicate that the rapidity of salbutamol's action should make it possible to shorten the duration of depressive episodes. It is concluded that the establishment of an antidepressant effect of such beta-adrenergic stimulants as salbutamol redirects attention to the noradrenergic hypothesis and away from a serotoninergic basis of depression. 10 references. (Author abstract modified)

003547 Stevenson, I. H.; Wilson, Nina M.; Schiff, A. A. Department of Pharmacology and Therapeutics, Ninewells Hospital, Dundee, Scotland **Implications of dose regimen and protein binding for plasma nortriptyline estimations.** Neuropharmacology (Oxford). 17(6):423-426, 1978.

The relationship between the steady-state plasma level of nortriptyline and clinical response was investigated in five patients being treated for mixed anxiety/depressive states and in six healthy volunteers. The steady-state plasma levels of nortriptyline in patients taking one tablet containing 1.5mg fluphenazine and 30mg nortriptyline daily were compared with those resulting from taking the same amount of drug in divided dose three times daily. Four of the five patients showed no significant difference in steady-state plasma levels of nortriptyline between the two for formulation treatment periods. Blood samples from the six healthy volunteers on the two treatment regimens, however, reveal that the once daily preparation exhibits a slow peaking effect. The percentage of unbound drug varied from 9.6to 3.2in the five patients studied. These variations could not be attributed to varying influences on the binding of nortriptyline caused by fluphenazine. 8 references.

003548 Warnock, J. M. T. no address **A controlled study of Trancopal in the treatment of sleep disturbances due to anxiety.** Journal of International Medical Research (Northampton). 6(2):115-120, 1978.

A total of 68 patients exhibiting sleep disburbances due to mild neurotic anxiety were treated for 2 weeks with a single night time dose of 400mg Trancopal or matching placebo under double-blind conditions. Patients kept a daily record of the quality of their sleep and the observer carried out a weekly rating of anxiety using a modified Hamilton scale. By day 7 patients receiving Trancopal had a significantly better rating for sleep and mean Hamilton scores for day time anxiety than the placebo group. Side-effects were minimal. It is concluded that for patients with sleep disturbances due to neurotic anxiety Trancopal is a well tolerated and effective alternative to the hypnotics. 5 references. (Author abstract)

003549 Zisook, S.; Rogers, Peggy J. Department of Psychiatry, P. O. Box 20708, University of Texas Medical School, Houston, TX **Efficacy of halazepam (SCH 12041) as an anxiolytic.** Current Therapeutic Research. 23(4):502-508, 1978.

The efficacy of halazepam (SCH-12041), a new benzodiazepine, in treating anxiety and tension was investigated. Halazepam was administered in a double-blind placebo controlled design to 51 outpatients for 6 weeks. Although most outcome measures favored halazepam over placebo, statistically significant results were obtained only at the end of the first week. Side-effects were observed to be minor and to diminish with time. It is concluded that halazepam is an effective, safe, and easily tolerated anxiolytic for the short-term treatment of anxiety. 4 references. (Author abstract)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

003550 Adams, David J.; Luders, Hans; Pippenger, Charles. 710 West 168th St., Room 5-560, New York, NY 10032 **Sodium valproate in the treatment of intractable seizure disorders: a clinical and electroencephalographic study.** Neurology. 28(2):152-157, 1978.

A 12 week study of clinical response, electroencephalographic (EEG) changes, and serum antiepileptic drug levels using sodium valproate (VAL) was undertaken. It was shown that VAL is a powerful adjunct in the treatment of intractable epilepsy. It was most effective in patients with generalized seizures, but no seizure type was totally resistant. No serious adverse effects were encountered; nausea was easily overcome by readjusting the drug dosage. In most cases the only EEG change was decrease of epileptiform activity, and this correlated well with decreased frequency of clinical seizures. These two features in turn were most often seen with a serum VAL level of 40mcg/ml or greater. Intoxication with VAL was accompanied by marked slowing of the background rhythms, but no increase in beta activity. Other modifications of the EEG were probably due to changes in the plasma levels of other durgs. Interactions between VAL and conventional antiepileptic drugs occur, so that serum concentrations of all drugs must be monitored in patients receiving VAL. 19 references. (Author abstract)

003551 Akiskal, Hagop S.; Webb, William L. Department of Psychiatry and Pharmacology, Center for the Health Sciences, University of Tennessee, Memphis, TN **Psychiatric diagnosis: exploration of biological predictors.** Mid-South Neuroscience Development Group Publication: 1. New York, SP Medical & Scientific Books, 1978. 493 p.

Areas of biological research with the potential for clinical application in the area of psychiatric diagnosis are discussed in a monograph based in part on the International Neuroscience Symposium, held in Memphis, Tennessee in 1975. Contributions are divided into the following major sections: clinical and biological criteria for psychiatric diagnosis; genetic principles in the

classification of psychiatric disorders; biochemical and pharmacological correlates; and neurophysiological and neuropsychological correlates.

003552 Bartova, D.; Nahunek, K.; Svestka, J. Psychiatric Clinic UJEP, Jihlavska 102, 657-15 Brno-Bohunica, Czechoslovakia **Pharmacological treatment of deviant sexual behaviour.** Activitas Nervosa Superior (Praha). 20(1):72-74, 1978

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during Janaury 1977, the pharmacological treatment of deviant sexual behavior is described. The treatment preparations examined were lithium, fluphenazine depot, and diethylstilbestrol (DES). Ss consisted of 105 sexual deviants. Only one patient suffered a criminal relapse. Side effects of DES include gynecomastia, depression, fatigue, disturbed potency, nausea, and acne. Lithium produced only nausea. Fluphenazine produced irreversible side effects. It is concluded that lithium is as effective as DES, and causes far fewer side effects. 5 references.

003553 Baxley, Gladys B.; Turner, Paul F.; Greenwold, Warren E. Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906 **Hyperactive children's knowledge and attitudes concerning drug treatment.** Journal of Pediatric Psychology. 3(4):172-176, 1978.

Individual, structured interviews with hyperactive boys were conducted to obtain information about their attitudes toward their drug treatment and their perceptions of the consequences of such treatment. The audiotaped responses of the 26 hyperactive boys, aged 6 years, 10 months to 16 years, 4 months, were content analyzed and categorized according to the percentage of subjects who gave the same (or similar) responses to each question. The responses show that the children are generally knowledgeable about the purpose of their medication, present generally mixed attitudes about having to take medication, but tend to associated not taking the medication with certain negative consequences. Findings may have some clinical relevance for the outcome of drug treatment of hyperactive children. 10 references. (Author abstract modified)

003554 Butler, Ian J.; Koslow, Stephen H.; Krumholz, Allan; Holtzman, Neil A.; Kaufman, Seymour. Department of Neurology, University of Texas Medical School, 6301 Alameda Road, Houston, TX 77021 **A disorder of biogenic amines in dihydropteridine reductase deficiency.** Annals of Neurology. 3(3):224-230, 1978.

A severe deficiency of dihydropteridine reductase (DHPR) in liver, brain, and cultured skin fibroblasts was demonstrated in a child with hyperphenylalaninemia and an atypical form of phenylketonuria. DHPR is required for the regeneration of the cofactor, tetrahydrobiopterin. The cofactor is essential in hydroxylation of aromatic amino acid precursors in the biosynthesis of neurotransmitters, serotonin, dopamine, and norepinephrine. In gray tissue at brain biopsy, dopamine was low at 3ng per gram of tissue, serotonin was barely detected, and norepinephrine appeared high at 1600 ng per gram. In cerebrospinal fluid, homovanillic (HVA) was low normal at 33 ng/ml, 5-hydroxyindoleacetic acid (5-HIAA) was low at 4.2ng/ml, and after a high dose of oral probenecid there was impaired accumulation of HVA to 128 ng/ml and 5-HIAA to 22.4ng/ml. When the patient was 22 months of age, treatment with dydroxylated aromatic amino acid precursors was initiated and after 3 months HVA and 5-HIAA levels were increased in cerebrospinal fluid. The apparent restoration of biogenic amines in brain appears to have delayed the rate of neurological deterioration. DHPR activity in cultured skin fibroblasts of children with persistent hyperphenylalaninemia should permit early diagnosis and treatment of this disorder. 51 references. (Author abstract)

003555 Campbell, Magda. New York University Medical Center, New York, NY **Pharmacotherapy.** In: Rutter, M., Autism: a reappraisal of concepts and treatment. New York, Plenum Press, 1978. 540 p. (p. 337-355).

Pharmacotherapy of autistic and schizophrenic children is examined. Topics discussed are the following: methodological issues; review of drug studies; therapeutic effects; clinical impressions; and untoward effects. It is suggested that considering the limited number of controlled drug studies among autistic and schizophrenic children, and considering that the sedative type of neuroleptics are thought to affect cognitive functions adversely in children, the use of available therapeutic psychoactive agents cannot be considered a long-term treatment approach, but rather as a temporary though often essential adjunct in the total treatment. It is felt that drugs should not be used if the risk and toxicity outweigh the possible therapeutic gains. 115 references.

003556 Diamond, Shirley G.; Markham, Charles H.; Treciokas, Leo J. Reed Neurological Research Center, UCLA School of Medicine, Los Angeles, CA 90024 **A double-blind comparison of levodopa, Madopa, and Sinemet in Parkinson disease.** Annals of Neurology. 3(3):267-272, 1978.

A 16 week study was undertaken to examine the effect of Madopa (levodopa plus benserazide in a 4:1 ratio) and Sinemet (levodopa plus carbidopa in 10:1 ratio) on patients with Parkinson disease suffering nausea or vomiting side effects of levodopa therapy and to compare the efficacy of the three preparations in controlling Parkinson symptoms. Following a control period on levodopa, 20 patients underwent four consecutive 4 week regimens: double-blind administration of levodopa or Madopa; single-blind administration of Madopa; double-blind administration of Madopa or Sinemet; and single-blind administration of Sinemet. Levodopa administration via Madopa or Sinemet was held to a fixed 20% of prior levodopa administration via Madopa or Sinemet was held to a fixed 20% of prior levodopa dosage. Almost all patients showed a great reduction in nausea and vomiting with both Madopa and Sinemet. Seventy percent of the patients showed improvement in disability compared to their levodopa baseline levels. Group means showed no difference between the improvement seen on Madopa and that of Sinemet. Examination of individual responses indicated that the majority of patients fared distinctly better on either Sinemet of Madopa than on levodopa. 15 references. (Author abstract modified)

003557 Dupont, E.; Hansen, Aa. Prange; Juul-Jensen, P.; Lundbaek, K.; Magnussen, I.; Olivarius, B. de Fine. Department of Neurology, Kommunehospitalet, Aarhus, Denmark **Somatostatin in the treatment of patients with extrapyramidal disorders and patients with EEG abnormalities.** Acta Neurologica Scandinavica (Kobenhavn). 57(6):488-493, 1978.

The potential therapeutic significance of somatostatin as a central nervous system depressant in the treatment of patients with extrapyramidal disorders and EEG abnormalities was tested. Sixteen patients with different extrapyramidal disorders and seven patients with various EEG abnormalities were tested with 2-hour somatostatin infusions and control infusions with saline. Somatostatin did not induce any improvement or deterioration of symptoms, signs, or EEG abnormalities in any patient. 12 references.

003558 Itil, T.; Mukhopadhyay, S. New York Medical College, New York, NY **Pharmacologic management of human violence.**

Modern Problems of Pharmacopsychiatry (Basel). 13:139-158, 1978.

The management of aggressive/violent behavior with chemicals is discussed. The sedative effects of antiaggressive drugs are associated with decreased motor activity, and effects on specific areas of the central nervous system. Psychostimulant drugs do not decrease psychmotor functions and have therapeutic effects on aggressive syndromes associated with behavioral disturbances, mental retardation, and hyperkinesia. Drugs such as diphenylhydantoin have a predominantly therapeutic effect on episodic behavior and aggressive/violent outburst. When the mode of action of these drugs on violent behavior was investigated, psychological tolerance was found to be subsequently increased. The mode of action of antiandrogens and how the hormonal properties of these compounds affects the complex psychophysiologic motor phenomenon of aggression is still under investigation. Although it has been determined that various treatments that modify aggression also change brain neurotransmitters, the link between a unique human behavior and a specific neurotransmitter has yet to be identified. Chemical treatment, based on empirical models, is recommended as a preferred treatment if the aggressive behavior has destructive potential.

003559 Janowsky, David S.; Leichner, Pierre; Clopton, Paul; Judd, Lewis L.; Parker, Donal; Huey, Leighton. Department of Psychiatry and Medicine, University of California at San Diego, Medical School, La Jolla, CA 92093 **Comparison of oral and intravenous methylphenidate.** Psychopharmacology (Berlin). 59(1):75-78, 1978.

The effects of oral methylphenidate (1.0mg/kg) and intravenous methylphenidate (0.5mg/kg) on the behavioral activation, pulse, blood pressure, and serum growth hormone of psychiatric inpatients were compared. Intravenous methylphenidate was considerably more effective than oral methlylphenidate in activating behavior and in increasing pulse and blood pressure. Although oral methylphenidate appeared to increase behavioral activation, this effect was not statistically significant. 10 references. (Author abstract modified)

003560 Lees, A. J.; Shaw, K. M.; Stern, G. M. Department of Neurology, University College Hospital, London WC1E 6AU, England **Baclofen in Parkinson's disease.** Journal of Neurology, Neurosurgery and Psychiatry (London). 41(8):707-708, 1978.

The effect of baclofen, an analogue of gamma-aminobutyric acid, on levodopa treated patients with Parkinson's disease was investigated. In a controlled trial, baclofen, at a mean dose of 45mg daily, significantly increased disability from Parkinsonism in 12 patients with the long-term levodopa syndrome. Peak dose choreoathetosis was not improved, but benefit was observed in all four patients with "off period dystonia." Adverse side-effects were common and severe, and included visual hallucinations, vomiting, and dizziness. 15 references. (Author abstract modified)

003561 Lewis, Melvin; Brown, Thomas E.; Hooven, Michael; O'Hare, Elizabeth. 333 Cedar Street, New Haven, CT 06510 **Medication in residential treatment: administration and clinical experiences.** Child Psychiatry and Human Development. 8(3):175-189, 1978.

A seven step clinical procedure for prescribing medication for children in residential treatment is described, and clinical procedures for monitoring medication are outlined. Experience during a 3 year period with antipsychotic medications, antianxiety medication, stimulants, antidepressants, sedatives, and anticonvulsive drugs is described with the aid of case studies. The use of medication for symptom control and to enable the child to gain a feeling of mastery of his or her symptoms is emphasized as a primary goal of drug treatment. 4 references. (Author abstract modified)

003562 Millichap, J. Gordon. 720 N. Michigan Ave., Chicago, IL 60611 **Growth of hyperactive children treated with methylphenidate.** Journal of Learning Disabilities. 11(9):567-570, 1978.

The growth of hyperactive children treated with methylphenidate was investigated. Methylphenidate in daily doses of 10mg to 20mg were administered for an average period of 16 months to 36 boys (5 to 10 years old) who showed hyperactive behavior associated with signs of minimal brain dysfunction and learning disorders. The percentile distributions of heights and weights recorded before and after treatment were not significantly different, and the rates of annual growth were above normal in 23 patients (64%). A possible growth stimulant effect was apparent in six patients between 5 and 8 years of age. It is concluded that relatively small doses of methylphenidate are well tolerated and do not cause growth suppression in hyperactive children with minimal brain dysfunction. 7 references. (Author abstract modified)

003563 Misurec, J.; Moravek, Z.; Nahunek, K. Faculty Hospital, Brno, Czechoslovakia **Lisurid (Lysenyl Spofa) in the treatment of organic psychosyndrome in involution.** Activitas Nervosa Superior (Praha). 20(1):87-88, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the use of lisurid in the treatment of organic psychosyndrome in involution is described. Following 2 months of therapy on 30 patients with organic psychosyndrome in involution, a comparison of lisurid with placebo showed that 28 symptoms had improved after the active drug and 7 after the placebo. Significant improvement in the following symptoms was noted: orientation, restlessness, suidical thoughts, and irritability. 3 references.

003564 Nahunek, K.; Kamenicka, V.; Misurec, J.; Slama, B.; Svestka, J.; Novotna, H. Psychiatric ClinicJihlavska 102, 657-15 UJEP, Brno-Bahunica, Czechoslovakia **Prophylactic lithium treatment of drug abuse.** Activitas Nervosa Superior (Praha). 20(1):70-72, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during Janaury 1977, prophylactic lithium treatment of drug abuse is described. Twenty one drug abuse patients were subdivided according to whether pretreatment with lithium reduced the emotional experience provided by their choice drug or not, and performance of these groups on psychological tests and EEG were compared. It is concluded that lithium prophylaxis could be beneficial for persons abusing psychostimulants.

003565 no author. no address **Malignant fever is now an office problem too.** Medical World News. 19(3):15, 1978.

Outpatient care of hyperthermia, now considered to be a stress related disease, is discussed. The outpatient maintenance program at the University of Nebraska is examined for its excellent record with haloperidol. Other drugs particularly dantrolene, a muscle relaxant have been winning acceptance in recent months in other outpatient maintenance programs. Given their very different chemical structures, it is concluded that these two drugs may have two different uses: dantrolene to prevent muscle related malignant hyperthermia; haloperidol to relieve emotional problems that potentiate the condition.

003566 O'Leary, Susan G.; Pelham, William E. Department of Psychology, SUNY, Stony Brook, NY 11794 **Behavior therapy and withdrawal of stimulant medication in hyperactive children.** Pediatrics. 61(2):211-217, 1978.

A study of seven hyperactive children was conducted to extend the evaluation of behavior therapy for children from whom stimulant medication was withdrawn. The focus was on home as well as school problems. Classroom activities of the children were observed for 1 week while the child was receiving medication and for 1 week without medication. An abbreviated form of the Conners Teacher Rating Scale was completed for each child. Mothers rated the behavior of their children on the Werry-Weiss-Peters Activity Scale. For 4 months following the initial 2 week assessment, an average of 18 sessions were conducted with the therapist. The effects of the withdrawal and treatment program suggest that behavior therapy is an effective and viable alternative intervention for some children who receive stimulant medication for the treatment of hyperactivity. Further research is recommended to determine whether this type of therapy can lead to improvement in academic achievement and long-term maintenance. 21 references.

003567 Pottenger, Margaret; McKernon, Janice; Patrie, Lewis E.; Weissman, Myrna M.; Ruben, Harvey L.; Newberry, Phyllis. Department of Psychology, University of Rochester, Rochester, NY 14627 **The frequency and persistence of depressive symptoms in the alcohol abuser.** Journal of Nervous and Mental Disease. 166(8):562-570, 1978.

A survey of 61 outpatients admitted to a mental health center for the treatment of alcoholism determined that a majority of them (59%) were clinically depressed. The depressive symptoms were rarely treated with antidepressant agents and, at 1 year followup, were found to persist even though the patients had attended the standard treatment program for alcoholics. There is a need for new treatment strategies that recognize the diagnostic heterogeneity of the alcoholic and that consider the use of appropriate psychopharmacological agents. 34 references. (Author abstract)

003568 Price, P. A.; Parkes, J. D.; Marsden, C. D. University Department of Neurology, Institute of Psychiatry, London, England **Sodium valproate in the treatment of levodopa-induced dyskinesia.** Journal of Neurology, Neurosurgery and Psychiatry (London). 41(8):702-706, 1978.

The effect of sodium valproate 1200mg daily on the disability of Parkinsonism and on levodopa-induced dyskinesias was assessed in a double blind crossover trial with matched placebo in 12 patients with Parkinson's disease. No objective change in the severity of Parkinsonism or dyskinesias was noted. However, six out of nine patients who completed the trial noted a slight to moderate improvement in their dyskinesias with no change in their Parkinsonism. Excess salivation improved in four subjects on sodium valproate. 17 references. (Author abstract)

003569 Puig-Antich, Joaquim; Greenhill, Laurence L.; Sassin, Jon; Sachar, Edward J. Department of Child Psychiatry, New York State Psychiatric Institute, 722 West 168 Street, New York, NY 10032 **Growth hormone, prolactin and cortisol responses and growth patterns in hyperkinetic children treated with dextro-amphetamine. Preliminary Findings.** Journal of Child Psychiatry. 17(3):457-475, 1978.

At the Annual Meeting of the American Academy of Child Psychiatry, held in Toronto, Ontario, October 21, 1976, a paper was presented in which the growth patterns of two groups of male hyperkinetic children are compared. One group was treated with d-amphetamine and the other group received phenothiazine. The subjects in the d-amphetamine group also underwent longitudinal neuroendocrine studies where they served as their own controls. Sleep related secretion of pituitary hormones and cortisol were measured at pretreatment, at 1 month, and at 6 months of continuous d-amphetamine administration. At the end of the first year, seven subjects treated with d-amphetamine were studied for growth changes and sleep endocrine measures, and the eight subjects treated with phenothiazine were studied for growth changes only. The significant findings are: growth retardation in the group treated with d-amphetamine; inhibition of mean sleep related prolactin secretion; and a highly significant correlation between loss of expected height percentile during the first year and decrease of mean sleep related prolactin at 6 months, as compared to baseline. The findings suggest that growth inhibition secondary to chronic d-amphetamine administration in hyperkinetic children might be mediated by inhibition of prolactin secretion. 48 references. (Author abstract modified)

003570 Rydzynski, Z.; Gruszczynski, W. Institute of Mental Hygiene of the Military Academy of Medicine, Lodz, Czechoslovakia **Treatment of alcoholism with psychotomimetic drugs. A follow-up study.** Activitias Nervosa Superior (Praha). 20(1):81-82, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, a follow-up study of the treatment of alcoholism with psychotomimetic drugs is presented. LSD-25 or psylocybine were administered to chronic alcoholics in conjunction with verbal psychotherapy. At 6 year followup, a satisfactory therapeutic effect was found in 58% of the patients. It is concluded that the best results can be expected in patients who reacted to the psychotomimetic shock with unpleasant feelings, had neurotic features with components of fear before the alcohol habit, were susceptible to suggestion, and reported aversion to alcohol in the period of drinking initiation.

003571 Saletu, B.; Grunberger, J.; Saletu, M.; Mader, R.; Volavka, J. Section of Pharmacopsychiatry, Psychiatrische Universitatsklinik, Wahringer Gurtel 74-76, Vienna, Austria **Treatment of the alcoholic organic brain syndrome with EMD 21657. A derivative of a pyritinolmetabolite: double-blind clinical, quantitative EEG, and psychometric studies.** International Pharmacopsychiatry (Basel). 13(3):177-192, 1978.

The efficacy of EMD 21657 was examined in the treatment of alcoholic organic brain syndrome (OBS). Nineteen patients were administered 3x300mg EMD and 21 patients were administered 3x1 dragee placebo for 6 weeks in a double-blind study utilizing clinical, psychometric, and quantitative EEG evaluations. Groups were matched for age, sex, weight, height, IQ, and alcohol anamnesis. While overall evaluation at the end of the treatment period failed to show significant between group differences, the clinical global impression scale and the OBS scale demonstrated that both groups showed significant improvement of their OBS, and that improvement with EMD therapy was significantly superior to that with placebo. Psychometric analysis also showed a significant superiority of EMD patients in memory, attention variability and concentration. EMD patients also showed greater psychomotor and mood/affect improvement compared to controls. While both groups showed changes in EEG activities, these changes were greater for EMD patients, particularly in augmentation of theta activity. It is concluded that EMD is a central nervous system effective drug with pronounced nootropic and slight thymotropic properties. 17 references. (Author abstract modified)

003572 Segal, M.; Hoppe, W.; Avison, R. G.; White, S. Halifax Hospitals Group, West Yorkshire, England **Alcoholism: practical aspects of management.** Nursing Times. 74(3):98-102, 1978.

Practical aspects of the management of alcoholism are discussed, with special emphasis given to physical aversion and motivation therapies. The case history of a patient who nearly

expired from the use of apomorphine is presented. The negative physical and social effects of alcohol consumption are discussed. Management modalities are reviewed, and the relaxation/aversion technique used by Blake is given preference. Disulfiram and chlormethiazole edisylate are discussed with reference to their pharmacology, efficacy, and side-effects. The use of the phrase "progressive alcohol dependency" as an alternative to the alarming and psychologically discouraging term "alcoholism" is encouraged. Individual and group psychotherapeutic measures and voluntary agency support appear to be the best means of combatting alcoholism as both a disease and a major social problem. 26 references.

003573 Shaffer, David; Hedge, Barbara; Stephenson, John. Department of Child Psychiatry, New York Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Trial of an alpha-adrenolytic drug (indoramin) for nocturnal enuresis.** Developmental Medicine and Child Neurology (London). 20(2):183-188, 1978.

A group of 14 enuretic schoolchildren were treated with a competitive alpha-adrenoceptor blocking substance, indoramin, in an attempt to mimic the known alpha-adrenolytic action of imipramine, a tricyclic antidepressant. Treatment in the two dosage schedules (20mg and 10mg) had no significant effect on night wetting frequency. The findings do not support the notion that the tricyclic drugs principally control enuresis through an effect on autonomic transmitters. 30 references. (Journal abstract)

003574 Singer, K.; Lo, C. W.; Tam, Y. K. Department of Psychiatry, University of Hong Kong, Queen Mary Hospital, Hong Kong **Comparative evaluation of hypnotic efficacy of flunitrazepam in psychiatric in-patients.** Acta Psychiatrica Scandinavica (Kobenhavn). 57(5):382-388, 1978.

Flunitrazepam (a new hypnotic of the benzodiczepine type) in 2mg and 4mg doses was compared with flurazepam 30mg and nitrazepam 10mg for hypnotic efficacy in a double-blind, multiple crossover trial involving 41 psychiatric inpatients. In the vast majority of comparisons involving a number of sleep parameters differences did not reach significance level. Flunitrazepam 4mg tended to produce the shortest latency time and the longest duration of sleep but also the most side-effects. Nitrazepam 10mg appeared to have a slight advantage over the other drugs in terms of patient preference. For severe sleep disturbance flunitrazepam 2mg tended to be the most satisfactory drug in terms of efficacy and paucity of side-effects. 3 references. (Author abstract)

003575 Smith, Christine M.; Swash, Michael. London Hospital Medical College, London E1 2AD, England **Possible biochemical basis of memory disorder in Alzheimer disease.** Annals of Neurology. 3(6):471-473, 1978.

The possible biochemical basis of memory disorder in Alzheimer diseas is discussed. The most common presenting symptom of Alzheimer disease is loss of short-term memory. Choline acetyltransferase, which is involved in the syntheis of acetylcholine, is depleted in the hippocampus in this disorder. Anticholinergic drugs administered to normal subjects can simulate some aspects of the memory defect seen in this disease. It is postulated that damage to a cholinergic neuronal pathway running to or from the hipoocampus underlies the memory disorder. Consequently, it may be possible to improve memory in patients with Alzheimer disease by pharmacological means. 37 references. (Author abstract modified)

003576 Suleman, D. E. St. Brendan's Hospital, Dublin, Eire **A comparison of the efficacy and acceptability of two formulations of injectable serenace in the treatment of states of excitement.** Journal of International Medical Research (Northampton). 6(3):193-198, 1978.

Serenace (haloperidol) was tested to compare the efficacy of its two formulations (dextrose and saline base) with 31 acute hospitalized patients, 29 females and 3 males, ranging in age from 19 to 57 years. All patients before treatment exhibited acute psychotic symptoms or acute exacerbations of chronic psychosis requiring immediate control. Serenace was given intramuscularly at a dose of 10mg or 20mg daily for a minimum of 7 days and in some cases was extended to 14 days. The results confirm no significant differences between the two preparations, either in their efficacy and acceptability or in the control of presenting symptoms. 8 references.

003577 Sullivan, John L.; Stanfield, Charles N.; Maltbie, Allan A.; Hammett, Elliott; Cavenar, Jesse O., Jr. Psychiatry Service, Veterans Administration Hospital, 508 Fulton Street, Durham, NC 27705 **Stability of low blood platelet monoamine oxidase activity in human alcoholics.** Biological Psychiatry. 13(3):391-397, 1978.

Data on blood platelet monoamine oxidase (MAO) acitivity in alcoholics was collected and studied over an extended time. Subjects in the study included alcoholic males between the ages of 23 years and 63 years with a 5 year to 40 year history of excessive alcohol consumption, and a control group. The results provide evidence that reduced platelet MAO activity in alcoholics is a relatively stable phenomenon, independent of ethanol consumption and proximate factors of the illness which are associated with excessive ethanol consumption. 24 references. (Author abstract modified)

003578 Sverd, J.; Kupietz, S. S.; Winsberg, B. G.; Hurwic, M. J.; Becker, L. Long Island Research Institute, Health Sciences Center, T-10, Stony Brook, NY 11794 **Effects of L-5-hydroxytryptophan in autistic children.** Journal of Autism and Childhood Schizophrenia. 8(2):171-180, 1978.

Behavioral effects of L-5-Hydroxytryptophan (L-5-HTP), administered in combination with carbidopa, were evaluated in three autistic children using direct behavioral observation and parent ratings. Children were assessed under each of four experimental conditions: baseline, placebo 1, L-5-HTP plus carbidopa, and placebo 2. During the 20 week study two children showed behavioral change that appeared to be unrelated to drug treatment. The findings do not support the hypothesis that a functional deficit in brain serotonin underlies the autistic syndrome. 21 references. (Author abstract)

003579 Ullman, Douglas G.; Barkley, Russell A.; Brown, H. Wesley. Department of Psychology, Bowling Green State University, Bowling Green, OH 43403 **The behavioral symptoms of hyperkinetic children who successfully responded to stimulant drug treatment.** American Journal of Orthopsychiatry. 48(3):425-437, 1978.

A sample of 36 hyperkinetic boys who successfully responded to drug treatment were compared with controls on a series of objective measures of activity and attentional problems in an effort to identify behavioral symptoms of successful drug responders. When hyperkinetic children with a history of successful responding to stimulants are removed from the drug, they appeared as a group to be more active than normal children regardless of the nature of the setting or type of activity evaluated. These children also proved to have shorter attention spans in free and resticted play and were less able to concentrate on a variety of experimental tasks. Results for individual children indicate that drug responders are probably no more homogeneous in their symptoms than the diverse population of hyperkinetic children in general. 29 references. (Author abstract modified)

003580 Vyborova, L.; Nahunek, K.; Drtilkova, I.; Misurec, J.; Slama, B. Psychiatric Clinic, Brno, Czechoslovakia **A controlled study of lisurid in hyperactive children.** Activitas Nervosa Superior (Praha). 20(1):86-87, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, a controlled study of lisurid in hyperactive children is described. The pacifying effects of lisurid on hyperactive children were investigated in a double-blind crossover design with 20 hyperactive, primarily encephalopathic children aged 5 to 12 years. The mean value of the global score of pathology decreased during lisurid treatment, and increased slightly during placebo. Lisurid improved concentration, school motivation, and school discipline, but there was still unsatisfactory control of emotional reactions after 14 days of lisurid treatment.

003581 Whalen, Carol K.; Collins, Barry E.; Henker, Barbara; Alkus, Stphen R.; Adams, Douglas; Stapp, Joy. Social Ecology, University of California, Irvine, CA 92717 **Behavior observations of hyperactive children and methylphenidate (Ritalin) effects in systematically structured classroom environments: now you see them, now you don't.** Journal of Pediatric Psychology. 3(4):177-187, 1978.

The behaviors in context which distinguish hyperactive from normal boys and methylphenidate from placebo states were studied in a naturalistic summer school program. Hyperactive boys on methylphenidate, hyperactive boys on placebo, and normal comparison boys were observed while two classroom dimensions were varied systematically in a 2 X 2 factoral design: 1) easy versus difficult materials, and 2) self-paced versus other paced activities. Compared to hyperactive boys on methylphenidate, the placebo group showed 1) lower rates of task attention; 2) higher rates of gross motor movement, verbalization, vocalization, noise, disruption, and social initiation; and 3) a more vigorous style of responding. No differences emerged between medicated hyperactive boys and normal peers. Group differences in specific behaviors varied with the two classroom dimensions, demonstrating the impact of medication by situation interactions. Significant relationships between teacher ratings and specific behavior observation categories were also found. Issues concerning ecological validity and scientific precision are discussed. 33 references. (Author abstract modified)

003582 Wolf, Sheldon M.; Forsythe, Alan. 1526 North Edgemont Street, Los Angeles, CA 90027 **Behavior disturbance, phenobarbital, and febrile seizures.** Pediatrics. 61(5):728-731, 1978.

The therapeutic administration of phenobarbital following febrile seizures in children was evaluated in terms of iatrogenic behavior distrubances. Of 109 children treated daily with phenobarbital following the first febrile convulsion, 42% developed a behavior disorder, usually hyperactivity. Daily phenobarbital therapy was prematurely discontinued in 54% of the children with behavior abnormality (20% of those treated). The behavior disturbance usually appeared within several months, was not correlated with high blood barbiturate levels, disappeared in 73% of children, an improved in all children when barbituate therapy was discontinued. Among children suffering from febrile seizures not given phenobarbital, the group that did not develop behavior disorders had a greater frequency of family history of seizures, especially febrile convulsions, and a lower frequency of preseizure behavior disturbance; abnormalities of pregnancy, labor, delivery, and neonatal period; delayed milestones; long seizures; abnormal results of neurological examination; abnormal EEG; and recurrent febrile seizures. 8 references. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

003583 Bachman, John Andrew. University of California, San Francisco **Factors contributing to cannabis intoxication and dependence. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 78-9188, HC$15. MF$7.50. 88 p. 1978.

Multiple regression analyses of self-report and nurses' observation data were conducted to determine the sources of variation in human subjects' responses to the prolonged oral administration of delta9-tetrahydrocannabinol (THC). The analyses focused on individual differences in subjects' backgrounds and bodyweights. Forty eight men received 30mg THC for at least 8 days following a period of 1-6 days in whch the dose was increased gradually or rapidly. Thirty seven subjects received pure THC in a sesame oil vehicle, and 11 received a crude extract of cannabis in an ethanol vehicle. Analyses demonstrate that the drug type and dosage schedule factors accounted for a significant proportion of the variance in the subjective and behavioral effects produced by THC. Drug type in conjunction with the subjects' personality characteristics, bodyweights, and condition just prior to THC withdrawal were associated significantly with the intensity that subjects and nurses reported changes following the cessation of THC administration. (Journal abstract modified)

003584 Bastecky, J.; Podrouzek, V.; Vinar, O. Chair of Psychiatry, Postgraduate Medical and Pharmaceutical Institute, 18100 Prage 8-Bohnice, Czechoslovakia **Alosteric changes in plasma proteins in healthy volunteers after administration of lysergamide.** Activitas Nervosa Superior (Praha). 20(1):82, 1978.

In a paper read at the Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, alosteric changes in plasma proteins in healthy volunteers after administration of lysergamide are reported. Mental changes of 10 healthy volunteers following adminstration of lysergamide were assessed using the 74 item questionnaire of Linton and Langs, and compared with changes in plasma proteins. It was found that, the greater the protein catalytical activity decreased, the greater the subjective response to lysergamide. A similar trend of protein denativation in schizophrenic patients is noted.

003585 Weingartner, H.; Murphy, D. L.; Stillman, R.; Eich, J. E. National Institute of Mental Health, Washington, DC 20032 **Mood state dependent learning.** Psychopharmacology (Berlin). 58(2):11, 1978

At the First International symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, mood state, dependent learning, and memory disociations were discussed. Memory dissociations occur when information is stored in one mood and retrieved in a disparate mood state. Experimental findings indicate that the subjective high produced by marihuana prior to storing or retrieving words determines the memory dissociation produced by the drug. Amphetamine treatment can also produce state dependent learning effects, but only in subjects who show robust changes in mood. Bipolar manic depressive patients show memory dissociations when retrieving self-generated events in mood states different from the storage state. When normal or depressed subjects engage in a task in which they perceive themselves as failing or succeeding, they frequently demonstrate mood changes; when the mood change occurs just prior to processings words or recalling words, dissociations of memory occur when the mood state is markedly different during storage and retrieval state.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

003586 Ananth, J. Faculty of Medicine, McGill University, Montreal, Quebec, Canada **Drug-induced dyskinesia: a critical review.** Indian Journal of Psychiatry (Lucknow). 20(1):31-36, 1978.

The research and clinical literature on drug-induced dyskinesia is reviewed in terms of incidence, etiology, and pathophysiology. The etiology of tardive dyskinesia is not well understood, but individual predisposition coupled with neuroleptic drug use are obvious factors. Even though compelling evidence is lacking, anticholinergic drugs apparently play a part. It is important to find out whether untreated Parkinsonian patients who are known to have lesions in substantia nigra have dopaminergenic hypersensitivity and also to note how many treated with L-dopa and anticholinergics develop dyskinesia and compare them with neuroleptic-induced dyskinesia. 47 references.

003587 Belmaker, R. H.; Ebstein, R. P.; Biederman, J.; Stern, R.; Berman, M.; van Praag, H. M. Jerusalem Mental Health Center-Ezrath Nashim, POB 140, Jerusalem, Israel **The effect of L-dopa and propranolol on human CSF cyclic nucleotides.** Psychopharmacology (Berlin). 58(3):307-310, 1978.

To define the possible neurotransmitter systems of origin of human cerebrospinal fluid (CSG) cyclic nucleotides, cyclic adenosine monophosphate (AMP) and cyclic guanosine monophosphate (GMP) were measured in Parkinson patients with and without L-dopa therapy and in schizophrenic patients before and after propranolol therapy. No effect of L-dopa or propranolol was found on CSF cyclic nucelotides. However, Parkinson patients showed a 40-50% reduction of CSG cyclic AMP and a 80-90% reduction of CSG cyclic GMP compared with schizophrenic patients. Implications of these findings are discussed. 20 references. (Author abstract modified)

003588 Bowmer, Christopher J.; Lindup, W. Edward. Department of Pharmacology and Therapeutics, University of Liverpool, P. O. Box 147, Liverpool L69 3BX, England **Binding of phenytoin, L-tryptophan and O-methyl red to albumin. Unexpected effect of albumin concentration on the binding of phenytoin and L-tryptophan.** Biochemical Pharmacology (Oxford). 27(6):937-942, 1978.

The binding of phenytoin and o-methyl red to human serum albumin (HSA) and the binding of L-tryptophan to bovine serum albumin were studied by equilibrium dialysis at 37 degrees, pH 7.4. Data for the binding of o-methyl red to HSA studied by variation of the concentration of either o-methyl red or albumin gave identical Scatchard plots. Scatchard plots of the data obtained forphenytoin and L-tryptophan, at constant ligand concentration and varying albumin concentrations, were unusual and had a positive slope. Values for the apparent association constant (k) and number of binding sites (n) could not be obtained from these plots, but it was apparent that n and/or k decrease as the albumin concentration increases. 49 references. (Author abstract modified)

003589 Ceder, G.; Dahlberg, L.; Schuberth, J. Psychiatric Research Center, University of Uppsala, Ulleraker Hospital, S-750 17 Uppsala 17, Sweden **Effects of 2-dimethylaminoethanol (Deanol) on the metabolism of choline in plasma.** Journal of Neurochemistry (Oxford). 30(6):1293-1296, 1978.

The effects of chronic oral administration of 30mM dimethylaminoethanol (DMAC) on the concentrations and turnover of putative acetylcholine precursors in the plasma and the cerebrospinal fluid (CSF) were investigated. Choline (Ch) and its labelled variants were measured by gas chromatography/mass fragmentography and lecithin, lysolecithin and sphingomyelin by spectrophotometric methods following separation by thin layer chromatography. No effects of DMAE on the phospholipids in the plasma separation by thin layer chromatography. No effects of DMAE on the phospholipids in the plasma of rabbits were found. The concentrations of Ch in the plasma of humans and rabbits and in the CSF of rabbits increased during the DMAE treatment. In the mouse labelled with deuterium Ch from the diet, DMAE increased the dilution of deuterium Ch in the plasma. Ch given by mouth to rabbits in the same dose as DMAE had no effects on plasma Ch. Intravenous infusion of 0.15M Ch for 60 min increased the concentrations of Ch in the CSF as well as in the plasma. It is concluded that DMAE increases plasma Ch by enhancing the formation of endogenous Ch, perhaps through the base exchange reaction. Whether or not DMAE also increases the availability of Ch directly in the brain cannot be decided. 15 references. (Author abstract)

003590 Curry, S. H.; Whelpton, R.; de Schepper, P. J.; Vranckx, S.; Schiff, A. A. Department of Pharmacology and Therapeutics, London Hospital Medical College, London E1 2AD, England **Plasma-fluphenazine concentrations after injection of long-acting esters.** Lancet (London). 1(8075):1217-1218, 1978.

Enanthate and decanoate, long acting esters of fluphenazine, were each given to two patients to study their time course in plasma. Results support the use of the two esters in different ways. The decanoate gave the more prolonged high concentrations, in keeping with its prescription for schizophrenia on a frequency less than that for the enanthate. The decanoate gave an early peak in keeping with its use in acute psychotic states. The enanthate gave highest levels in 2-5 days, and this and the early high peak after the decanoate may have importance for unwanted extrapyramidal effects. 3 references. (Author abstract modified)

003591 Curtis, Jerry L. Central State Hospital, Milledgeville, GA **In vivo conversion of mesoridazine to thioridazine.** Research Communications in Psychology, Psychiatry and Behavior. 3(3):285-286, 1978.

The in vivo conversion of mesoridazine to thioridazine is reported. Thioridazine is known to be converted in vivo to mesoridazine, but the reversal of the process has not been previously observed. Data was obtained from the blood of a 29-year-old White female weighing 34 kilograms, diagnosed as schizophrenic, and taking only mesoridazine. Though there is an apparent reversal of thioridazine to mesoridazine, the clinical significance, if any, is unknown. 3 references.

003592 Di Chiara, Gaetano; Gessa, Gian Luigi. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Pharmacology and neurochemistry of apomorphine.** Advances in Pharmacology and Chemotherapy. 15:87-160,1978.

The physiological, neurochemical, pharmacological, and clinical effects of apomorphine are reviewed. The following areas are discussed on the basis of apomorphine research: its chemical pharmacology; emetic effects; behavioral effects; neuropharmacological effects; cardiovascular effects; endocrine effects; its effects on the dopamine, norepinephrine, serotonin, and acetylcholine systems and on adenyl cyclase; and emesis in man, movement disorders, and psychomotor effects. Other dopamine receptor agonists also are considered. 489 references.

003593 Erdos, Ervin G.; Johnson, Alice R.; Boyden, Nit T. Department of Pharmacology and Internal Medicine, University of Texas Health Science Center at Dallas, Dallas, TX 75235 **Hydrolysis of enkephalin by cultured human endothelial cells and by**

purified peptidyl dipeptidase. Biochemical Pharmacology (Oxford). 27(5):843-848, 1978.

The hydrolysis of enkephalin by cultured human endothelial cells and by purified peptidyl dipeptidase was examined. Results indicate that the rapid inactivation of enkephalins may be due to at least two different enzymes present in tissues. A peptidyl dipeptidase that is a component of plasma membrane of various cells may degrade enkephalins by liberating C-terminal dipeptide. In addition, an aminopeptidase in endothelial cells may cleave peptides that are taken up as blood flows past the endothelial surface. 11 references.

003594 Gentil, V.; Alevizos, B.; Lader, M. Instituto de Ciencias Biomedicas U.S.P. C.P. 4365, Sao Paulo, Brazil **Effects of single doses of tranylcypromine on platelet MAO and amine uptake in normal subjects.** Biochemical Pharmacology (Oxford). 27(8):1197-1201, 1978.

Twelve normal volunteers were given single doses of dl-tranycypromine (10 and 20mg) and placebo under double-blind conditions, using a balanced crossover design. Blood samples taken prior to treatment and at intervals thereafter were assayed for platelet monoamine oxidase (MAO) activity and platelet uptake of 5-hydroxytryptamine, dopamine, and metaraminol. Platelet MAO activity was markedly and significantly reduced after both doses of tranylcypromine and remained low for at least 24 hours. By contrast, amine uptake into the subject's platelets was slightly but not significantly reduced. In vitro studies yielded parallel results; tranylcypromine was much more potent in inhibiting platelet MAO than platelet amine uptake. Therefore, it seems unlikely that the antidepressive activity of the MAO inhibitors might correlate more closely with their ability to inhibit catecholamine uptake than with their power to inhibit MAO, as has been suggested. 21 references. (Author abstract)

003595 Gilbert, John N. T.; Nelmes, Philip T. J.; Powell, John W. Department of Pharmaceutical Chemistry, School of Pharmacy, 29/39, Brunswick Square, London WC1N 1AX, England **The synthesis and urinary estimation of N-hydroxyaprobarbitone.** Journal of Pharmacy and Pharmacology (London). 30(3):173-175, 1978.

N-Hydroxyaprobarbitone was synthesized by oxidation of aprobarbitone and a method was developed for its estimation in urine. Aprobarbitone (100mg) was administered orally to a male volunteer, and urine was collected for the following 3 days. Unchanged aprobarbitone excreted in the urine accounted for 9% of the drug, while N-hydroxyaprobarbitone accounted for only 3.6% of the ingested drug. As N-hydroxyaprobarbitone was found to be only a minor metabolite in the human metabolism of aprobarbitone, it is clear that N-hydroxylation cannot fully account for the metabolic fate of barbiturates in humans. 8 references.

003596 Greenblatt, David J.; Shader, Richard I.; Weinberger, Daniel R.; Allen, Marcia D.; MacLaughlin, Dean S. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Effect of a cocktail on diazepam absorption.** Psychopharmacology (Berlin). 57(2):199-203, 1978.

The influence of ethanol on the rate and extent of diazepam absorption was studied. Six healthy volunteers ingested a single 5mg tablet of diazepam with a typical ethanol containing cocktail (1.5oz of 80 proof vodka plus 4oz orange juice) or with orange juice alone. Diazepam concentrations in multiple plasma samples drawn from 15 minutes to 24 hours after each dose were determined by electron capture gas/liquid chromatography. Mean values of pharmacokinetic variables for diazepam taken with and without ethanol, respectively, were: peak plasma diazepam concentration, 221 vs 208ng/ml; time of peak concentration, 0.79 vs 1.79 hours after dosing; apparent lag time prior to start of absorption, 16.5vs 26.2minutes; apparent first order absorption half-life, 19.3vs 34.6minutes. The completeness of diazepam absorption, judged by the area under the 24 hour plasma concentration curve, was nearly identical for the two conditions. It is concluded that coadministration of diazepam with ethanol tended to slow the rate of diazepam absorption but did not influence the completeness of absorption. 21 references. (Author abstract modified)

003597 Gruen, Peter H. 115 East 82nd Street, New York, NY 10028 **The prolactin response in clinical psychiatry.** Medical Clinics of North America. 62(2):409-424, 1978.

Certain applications of the plasma prolactin measurement to the neuropharmacologic study of antipsychotic drug action and to the neurochemical (dopamine) study of the brain in schizophrenia are reviewed. The prolactin response reliably reflects the antidopaminergic properties of neuroleptic drugs. It is a graded response over a limited range, and within that range it predicts the clinical potency of neuroleptic drugs in man as well as any other currently available method in animals or man. The limited range of sensitivity of the prolactin responses appears to limit the possibilities of correlating with clinical response, since the lowest treatment doses in schizophrenia generally would produce maximal prolactin response. However, the prolactin response may be useful in identifying cases of noncompliance or inadequate bioavailability of a neuroleptic drug because of metabolic disturbances. 144 references.

003598 Hosobuchi, Yoshio; Li, Choh Hao. Department of Neurological Surgery, University of California, San Francisco, CA 94143 **The analgesic activity of human beta-endorphin in man.** Communications in Psychopharmacology. 2(1):33-37, 1978.

The ability of human beta-endorphin to relieve intractable pain in three patients on a neurological surgery service was tested. Intraventricular administration of human beta-endorphin resulted in pain relief of a significant nature. A single dose of 200 mcg of the peptide was the minimum effective dose with no observable side effect. The pain relief thus produced was accompanied by alterations of the acute pain threshold as measured by a thermal dolorimeter. Both effects were reversed by the specific opiate antagonist, naloxone. It is concluded that possible tolerance development observed in animals has to be tested in humans before the true clinical value of beta-endorphin as an analgesic agent can be evaluated. 10 references. (Author abstract modified)

003599 Kamenetskiy, V. K. Leningradskiy psikhonevrologicheskiy institut im. V. M. Bekhtereva, Leningrad, USSR **/Study of the treatment of vascular Parkinson's disease with metamizyl./** Opyt lecheniya metamizilom sosudistogo parkinsonizma. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 78(3):365-370, 1978.

Forty five patients with various forms of vascular Parkinson's disease were treated with metamizyl at a neurological clinic. Ss were between the ages of 50 and 80 and had been suffering from the disease for between 1 and 10 years. It was established that with treatment of a month's duration, metamizyl exerts a positive effect against the development of such symptoms as rigidity, bradykinesia and tremor in mild and moderate cases of lesion. In most cases the drug was effective in doses of .001g three times a day, and in isolated cases, .001g six times a day. In the majority of patients no significant side-effects were noted, but some experienced mild vertigo and dryness of the mouth. The treatment's effectiveness could be observed beginning 2 days to 2 weeks after the initial dosage and lasting throughout the period of treatment and usually for a short time thereafter.

Metamizyl is a moderate sedative and has a spasmolytic and hypotensive effect beneficial to patients with vascular parkinsonism. 9 references. (Journal abstract modified)

003600 Karniol, I. G.; Dalton, J.; Lader, M. H. Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England **Acute and chronic effects of lithium chloride on physiological and psychological measures in normals.** Psychopharmacology. 57(3):289-294, 1978.

Six healthy volunteers were given two oral doses of lithium chloride (16 and 32mM) and placebo sodium chloride (32mM) in a double-blind standardized procedure, with a 1 week interval between treatments. Compared to sodium, lithium produced a decrease in subjective well-being, decrease of skin conductance fluctuations, and increase in plasma calcium concentrations. Dose related effects were maximal at the first hour after ingestion, decreasing or disappearing at 3-5 hours. Most effects did not correlate with plasma or erythrocyte lithium concentrations, but drug effects and feelings of nausea were highly correlated. In a second experiment, six healthy volunteers were given 16mM of lithium chloride or sodium chloride twice a day for 1 week with a 2 week interval between treatment weeks. Compared to placebo, lithium produced feelings of impairment, an increase in EEG slow waves and of auditory evoked response variability, a deficit in long-term memory, and an increase in plasma magnesium concentrations. Most lithium effects did not correlate with plasma or erythrocyte lithium concentrations. 25 references. (Author abstract modified)

003601 Man, Pang L.; Chen, Calvin H. 41001 Seven Mile Road, Northville, MI 48167 **Plasma levels of neuroleptics vs clinical responses.** Psychosomatics. 19(3):151-156, 158-159, 1978.

The correlation of blood plasma levels to clinical responses of all available psychotropic drugs and related medications (antipsychotic drugs, antidepressants, antianxiety drugs, sedatives, stimulants) is summarized. The optimal therapeutic plasma levels are tabulated. Ten factors that influence the clinical response (dosage schedule, route of administration, optimal therapeutic level, paradoxical phenomenon, cumulativ effect, side effects, drug interaction, age, blood-brain barrier, and heredity) are discussed. 61 references. (Author abstract modified)

003602 Muskiet, F. A. J.; Jeuring, H. J.; Teelken, A. W.; Wolthers, B. G.; Lakke, J. P. W. F. Centraal Klinisch Chemisch Laboratorium, Academisch Ziekenhuis Groningen, Oostersingel 59, Groningjen, the Netherlands **Identification and quantification of 3-methoxy-4-hydroxyphenyllactic acid (VLA) in cerebrospinal fluid and 3-methoxy-4-hydroxyphenylpyruvic acid (VPA) in the urine of parkinsonian patients treated with L-DOPA.** Journal of Neurochemistry (Oxford). 31(5):1283-1288, 1978.

The identification and quantification of 3-methoxy-4-hydroxyphenyllactic acid (VLA) in cerebrospinal fluid (CSF) and of 3-methoxy-4-hydroxyphenylpyruvic acid in the urine of parkinsonian patients treated with L-3,4-dihydroxyphenylalanine (L-DOPA) with or without a peripheral decarboxylase inhibitor are described. Data are also given for other catecholamine and catecholamine precursor metabolites in urine and CSF. Analyses weer preformed by gas chromatography with flame ionization or mass spectrometric detection. Results suggest that following the administration of L-DOPA plus a peripheral decarboxylase inhibitor, VLA must be considered as a quantitatively important metabolite of L-DOPA in CSF. 12 references. (Author abstract)

003603 Ogiso, Taro; Masuda, Hiroyuki; Oue, Sanae. Gifu College of Pharmacy, Mitahora, Higashi-5-6-1, Gifu, Japan **Effect of drugs on human erythrocytes -- 4. Protecting effect of dextran on drug-induced hemolysis.** Biochemical Pharmacology (Oxford). 27(8):1263-1268, 1978.

Dextrans (molecular weight of 7,600, 18,500, and 23,200) were used to produce a protecting effect on hemolysis induced by chlorpromazine and clemastine in vitro. Electron microscopic observations indicated that addition of the dextrans at higher concentrations to the cells partially prevented cell shrinkage. Most of the cells retained smooth spheres at 0.8mM chlorpromazine, a concentration that produced 100% hemolysis in the absence of dextrans. Although the dextrans had no stabilizing effect on the cell membrane, they strongly inhibited the diffusion of hemoglobin and potassium and decreased quantities of the drug molecules absorbed to the cells. There was a good correlation between the viscosity of the dextrans and the protecting effect on drug-induced hemolysis. 38 references. (Author abstract modified)

003604 Perry, Thomas L.; Hansen, Shirley. Department of Pharmacology, University of British Columbia, Vancouver, Canada V6T 1W5 **Biochemical effects in man and rat of three drugs which can increase brain GABA content.** Journal of Neurochemistry (Oxford). 30(4):679-684, 1978.

The biochemical effects of three drugs which can elevate brain gamma-aminobutyric acid (GABA) were assessed in rats and in humans. In rats, brain GABA content was significantly elevated by aminooxyacetic acid (AOAA) doses of 10mg/kg/day but not by 5mg/kg/day. Approximately four times as much AOAA was required by mouth as by parenteral injection to raise brain GABA content. Intraperitoneal injection of sodium dipropylacetate (DPA, 400mg/kg) increased brain GABA and lowered brain aspartate content significantly, while oral DPA (350mg/kg/day) produced no alterations of any amino acids in rat brain. In humans, isonicotinic acid hydrazide (INH, 10-21mg/kg/day) increased concentrations of beta-alanine and ornithine in plasma, as well as urinary excretion of beta-alanine. DPA had no such effect. AOAA in oral doses ranging from 1.25 to 5.0mg/kg/day increased plasma concentrations of beta-alanine, ornithine, beta-aminoisobutyric acid, proline, and hydroxyproline, and produced massive urinary excretion of beta-alanine, beta-aminoisobutyric acid, and taurine. AOAA, in the lowest dose used, appeared more effective than INH as an inhibitor of GABA aminotransferase in humans and may prove useful in the treatment of neurological diseases in which brain GABA is deficient. 27 references. (Author abstract modified)

003605 Phillipson, Oliver; Baker, Janet; Sebastianpillai, Frank; Sheppard, Graham; Brook, Peter. Department of Anatomy, Karolinska Institutet, S 104 01 Stockholm 60, Sweden **Disappearance of chlorpromazine from plasma following drug withdrawal.** Psychological Medicine (London). 8(2):331-334, 1978.

The rate of disappearance of chlorpromazine following the discontinuation of medication was investigated in a group of 17 chronically hospitalized patients. In all cases, plasma chlorpromazine and its metabolites, as measured by a gas chromatographic procedure, were found to disappear rapidly during the first week following cessation of medication. These results are in agreement with other findings and indicate that the compound is cleared rapidly from circulation despite the relatively large tissue stores of the drug that exist following long-term treatment. It is suggested that probability of relapse following cessation of chlorpromazine therapy is an important clinical question for future studies. 12 references. (Author abstract modified)

003606 Rysanek, K.; Bilkova, B.; Spankova, H. Third Clinic of Internal Medicine, Pekarska 53, 65691 Brno, Czechoslovakia **The effect of chlorpromazine, some tricyclic antidepressants and insulin on the action of cyclic AMP and adenosine metabolism.** Activitas Nervosa Superior (Praha). 20(1):64-66, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the effects of chlorpromazine, some tricyclic antidepressants, and insulin on the action of cyclic AMP (c-AMP) and adenosine metabolism are described. Results indicate that chlorpromazine, dosulepine, imipramine, and nortriptyline do not affect either spontaneous phosphorylation of human erythrocyte membranes or c-AMP activated phosphorylation. Insulin was the only substance which exhibited a distinct inhibitory effect onthe c-AMP activated membrane phosphorylation. 10 references.

003607 Schubert, David. Neurobiology Laboratory, Salk Institute, P.O. Box 1809, San Diego, CA 92112 **NGF-induced alterations in protein secretion and substrate-attached material of a clonal nerve cell line.** Brain Research (Amsterdam). 155(1):196-200, 1978.

The effect of nerve growth factor (NGF) on the synthesis of extracellular proteins was examined by isolation of a nerve cell line, PC12, with both experimental and control cultures grown in identical states. The data indicate that NGF alters the release of cellular proteins into the culture medium and the deposition of proteins on the culture dish. It is reported that dibutyryl adenosine-3',5'-monophosphate (DBcAMP) mimics the effect of NGF on these two classes of macromolecules. It is concluded that cAMP mediates at least some effects of NGF on PC12 cell line. Some of the NGF-induced changes in secreted and substrate attached material proteins which are reported may be directly involved in the alterations in cellular adhesiveness caused by nerve growth factor. 16 references.

003608 Stahl, Stephen M.; Meltzer, Herbert Y. Department of Neurology, University of California School of Medicine, San Francisco, CA 94143 **A kinetic and pharmocologic analysis of 5-hydroxytryptamine transport by human platelets and platelet storage granules: comparison with central serotonergic neurons.** Journal of Pharmacology and Experimental Therapeutics. 205(1):118-132, 1978.

The mechanisms wherby human pplatelets transport serotonin (5-HT) were explored by determining the initial velocity of 5-HT uptake over a wide range of 5-HT concentrations. Total 5-HT transport could be resolved into a saturable high affinity/low capacity active transport system plus nonsaturable passive diffusion. Previous kinetic analyses of 5-HT transport into platelets and brain slices have been found to be in error and the correct kinetic constants were recalculated. The saturable active uptake of 5-HT into human platelets is directly susceptible to inhibition by several pharmacologic agents which do not inhibit the nonsaturable passive diffusion nor the nonsaturable granular transport of 5HT. On the other hand, granular binding of 5-HT is directly susceptible to inhibition by pharmacologic agents which do not directly inhibit saturable active uptake nor nonsaturable passive diffusion of 5-HT. It is noted that at low concentrations of 5-HT, the pharmocological and biochemical properties of total 5-HT transport are determined mostly by the saturable high affinity active membrane transport system for 5-HT; at high concentrations of 5-HT, the properties of 5-HT accumulations by platelets are determined mostly by the granular storage mechanism. The hypothesis that the platelet can serve as a model for 5-HT transport by central nervous system neurons is supported by comparisons of the kinetic biochemical and pharmacological characteristics of 5-HT transport in platelets and brains. 37 references. (Author abstract modified)

003609 Sweeney, Donal; Pickar, David; Redmond, D. E., Jr.; Maas, James. Clinical Research Ward, Department of Psychiatry, Yale University, New Haven, CT 06508 **Noradrenergic and dopaminergic mechanisms in Gilles de la Tourette syndrome.** Lancet (London). 1(8069):872, 1978.

Functional interactions between noradrenergic and dopaminergic systems in Gilles de la Tourette syndrome are discussed with reference tp neurobiological findings in a 49-year-old woman. Data showing the relation between muscular tics and the presence of 3-methoxy-4-hydroxyphenethyleneglycol in the urine are presented. Support for a direct relationship between tics and overactivity of brain dopamine systems stems from evidence that haloperidol reduces tic frequency. Noradrenergic agonists may be useful as adjunctive therapy in cases where tics are not alleviated by the administration of haloperidol. 8 references.

003610 Tanaka, Masatoshi; Isozaki, Hiroshi; Inanaga, Kazutoyo; Ogawa, Nobuya. Department of Pharmacology, Kurume University School of Medicine, Kurume 830, Japan **The effects of a new benzodiazepine derivative, ID-540, on the averaged photopalpebral reflex in man.** Psychopharmacology (Berlin). 58(3):217-222, 1978.

The effects of a recently introduced benzodiazepine derivative, 7-chloro-5-(2-fluorophenyl)-1-methyl-1H, 1.4-benzodiazepin-2(3H)-one (ID-540), on the averaged photopalpebral reflex (PPR), subjective symptoms, and serum levels of ID-540 and its principal metabolite, N-desmethyl-ID-540 were investigated in six male students following an oral dose of 0.5mg or placebo. The peak latencies of PPR showed a statistically significant prolongation, with maximum level at 3 hours after administration and recovery to the initial level within 4 hours. The amplitude of PPR failed to show a definite response to the drug. Serum concentrations of ID-540 reached a peak level 2 to 3 hours after administration and then decreased at 4 hours. N-desmethyl-ID-540 exhibited a slow, gradual rise in serum. The latencies of PPR were positively correlated with the serum level of ID-540 but not with the N-desmethyl-540. It is concluded that the PPR test may be a useful method for predicting the clinical effects of psychotropic drugs. 12 references. (Author abstract modified)

003611 Trimble, Michael. National Hospital for Nervous Diseases, Queen Square, London WC1N 3BG, England **Non-monoamine oxidase inhibitor antidepressants and epilepsy: a review.** Epilepsia. 19(3):241-250, 1978.

The literature dealing with the convulsant effects of the antidepressant drugs of the nonmonoamine oxidase inhibitor variety is reviewed. Most of these drugs lower the seizure threshold and may precipitate seizures even at normal therapeutic doses. The pathophysiology of antidepressants that have at least epileptogenic potential or may even be anticonvulsant are highlighted. The clinical difficulties regarding administration of antidepressant drugs to epileptic patients are noted and some practical advice is presented. 71 references. (Author abstract)

003612 Weingartner, H.; Sitaram, N.; Gillin, J. C.; Murphy, D. L.; Eich, J. E. National Institute of Mental Health, Washington, DC 20032 **Memory consolidation and cholinergic state-dependent learning in man.** Psychopharmacology (Berlin). 58(2):11, 1978

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, memory consolidation and cholinergic state dependent learning were reviewed. Changes in cholinergic activity prior to or just after information processing induce state dependent storage (SDS) and retrieval (SDR) of information. Intravenous physostigmine (.5mg) produces SDS/SDR when subjects are treated with the drug or placebo just before or after processing sets of categorized words. Recall is more complete when storage and retrieval state are the same, and dissociations in memory in the disparate retrieval state can be reversed by providing cues at the time of retrieval. Subjects treated with physostigmine 5 minutes after storage and again just before remembering 3 hours later demon-

strate more complete recall than when retrieval occurs following placebo treatment. This poststimulus processing consolidation stage state dependent learning effect can be reversed by subject generated cues during recall. Similar findings were obtained in experiments with arecholine, a cholinergic agonist.

003613 Widerlov, Erik; Wide, Leif; Sjostrom, Rolf. Psychiatric Research Center, Ulleraker Hospital, University of Uppsala, S-750 17 Uppsala, Sweden **Effects of tricyclic antidepressants on human plasma levels of TSH, GH and prolactin.** Acta Psychiatrica Scandinavica (Kobenhavn). 58(5):449-456, 1978.

The effects of tricyclic antidepressants on human plasma levels of thyrotropin (TSH), growth hormones (GH), and prolactin are examined. Six healthy male volunteers were given 25mg of chlorimipramine three times daily or 25mg of nortriptyline three times daily for 7 days in a randomized order. It is reported that the tricyclic antidepressants did not exert any influence on plasma hormonal levels compared with no treatment conditions. Diminished TSH responses following daily injections of thyrotropin releasing hormone (TRH) were demonstrated in endogenously depressed and chronic schizophrenic patients. A decreased TSH response was observed in healthy volunteers after a second TRH injection with an interval of 2 days bwtween the TRH injections. It is concluded that there may be a diminished sensitivity or a decreased availability of hormone receptors following repeated TRH injections. 23 references. (Author abstract modified)

003614 Wode-Helgodt, B.; Borg, S.; Fyro, B.; Sedvall, G. Dept. of Psychiatry, St. Goran's Hospital, S-112 81 Stockholm, Sweden **Clinical effects and drug concentrations in plasma and cerebrospinal fluid in psychotic patients treated with fixed doses of chlorpromazine.** Acta Psychiatrica Scandinavica (Kobenhavn). 58(2):149-173, 1978.

The clinical effects of chlorpromazine (CPZ) administered in a double-blind experiment in one of three doses (220, 400, or 600mg) were examined in 44 psychotic patients. The relationships between the effects and the CPZ concentrations in plasma and cerebrospinal fluid (CSF) were analyzed. Antipsychotic and side-effects were rated according to the Comprehensive Psychopathology Rating Scale (CPRS) and the Simpson and Angus scale. CPZ concentrations were measured by a mass fragmentographic method. Treatment with CPZ resulted in a significant reduction of morbidity scores, without any clear dose relation. The outcomes were more favorable in women than in men. Extrapyramidal side-effects but not somnoloence were positively dose related. Antipsychotic effects were positively related to the dose of CPZ as well as the CPZ concentrations in plasma and CSF. The greatest number of significant correlations between CPZ concentration in CSF and the morbidity scores were seen after 2 weeks of treatment. The results indicated marked clinical improvement with CPZ concentrations above 1ng/ml in CSF and 40ng/ml in plasma. Correlations between CPZ concentrations and clinical improvement declined somewhat after 4 weeks of treatment. Extrapyramidal symptoms were significantly related to CPZ concentrations. Somnolence was significantly related to CPZ concentrations in CSF. 46 references. (Author abstract)

14 MECHANISM OF ACTION: BEHAVIORAL

003615 Anisman, Hymie; Bignami, Giorgio. Department of Psychology, Carleton University, Ottawa, Ontario, Canada **Psychopharmacology of aversively motivated behavior.** New York, Plenum, 1978. 564 p. $35.00

The neurochemical mechanisms underlying aversively motivated behavior and drug effects thereon are discussed. Individual chapters cover the following topics: aversively motivated behavior as a tool in psychopharmacologic analysis; behavioral genetics and animal learning; behavioral correlates of neurochemical changes elicited by stress; cholinergic mechanisms and aversively motivated behaviors; monoamines and aversively motivated behaviors; hallucinogens; effects of neuroleptics, ethanol, hypnotic sedatives, tranquilizers, narcotics, and minor stimulants in aversive paradigms; stimulus attributes of drugs; and a comparative neurochemical, pharmacological, and functional analysis of aversively motivated behaviors.

003616 Barchas, Jack D.; Akil, Huda; Elliott, Glen R.; Holman, R. Bruce; Watson, Stanley J. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **Behavioral neurochemistry: neuroregulators and behavioral states.** Science. 200(4344):964-973, 1978.

The relation of neuroregulators in mammalian systems to emotional states and drives is discussed, and the multiple ways in which information regarding neuroregulators has developed and has affected the general concepts and approaches in behavioral neurochemistry are demonstrated. Examples of some problems, substances, and hypotheses which have received particular attention are given, and clinical problems with which neuroregulators have been linked are considered. Some of the recent work dealing with opiate-like substances in the brain, which may function as neuroregulators, is considered as a case that demonstrates the rapid advances within the general field. Some general considerations related to health maintenance problems are discussed. It is shown that there is compelling evidence that behavioral events alter neurochemical function and that altered neurochemical function can change behavior. The work is changing long-held concepts about severe mental disorders and the treatment of them. 83 references. (Author abstract modified)

003617 Barry, Herbert, III. Department of Pharmacology, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA 15213 **Stimulus attributes of drugs.** In: Anisman, H., Psychopharmacology of aversively motivated behavior. New York, Plenum, 1978. 564 p. (p. 455-485).

Several types of evidence for the punishing effects of the unconditioned drug stimulus are reviewed. The three stimulus attributes of drugs which are identified are 1) the strong physiological effect (an aversive unconditioned stimulus), 2) the sudden relief of other aversive drives (a reinforcing unconditioned stimulus), and 3) the discriminative signal or dissociative effect (a conditioned stimulus associated with a different unconditioned stimulus). Voluntary self-administration of drugs by laboratory animals and by humans is explained as a method for reducing other, ongoing drives. A proposed model for the discriminative drug stimulus locates the effect of a particular drug on several dimensions of difference from the nondrug condition. 98 references.

003618 Berger, Philip A. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **Medical treatment of mental illness.** Science. 200(4344):974-981, 1978.

Some of the practical, scientific, and ethical aspects of the medical treatment of mental illness are discussed. A description of the predrug era is followed by a discussion of the impact of recent therapeutic innovations. Three major psychiatric disorders are described: schizophrenia, depression, and mania. Evidence for the efficacy of the important current drug treatments for these disorders, practical aspects of treatment, and critical evaluations of their hypothesized biochemical mechanisms of action are described. The ethical problems created by the drug treatments of mental disorders are outlined. 46 references.

003619 Burns, David; Brady, John Paul; Kuruvilla, Kurien. Department of Psychiatry, University of Pennsylvania, Philadel-

phia, PA 19104 **The acute effect of halopheridol and apomorphine on the severity of stuttering.** Biological Psychiatry. 13(2):255-264, 1978.

The acute effect of haloperidol and apomorphine on the severity of stuttering was investigated in 12 subjects who were not in treatment at the time of evaluation. A single 0.5mg haloperidol injection was found to increase fluency in 9 of 12 subjects, as compared with saline placebo. The average improvement in those subjects who improved was 25% on reading and 40% on spontaneous speech. Side-effects from this dose of haloperidol were minimal. The effects of apomorphine on speech were not statistically significant, but increased fluency was seen in a number of subjects on the reading test. The results of this study suggest that acute drug evaluation studies may be valuable in determining the effects of various psychotropic agents on the severity of stuttering. 32 references. (Author abstract modified)

003620 Cianchetti, C.; Masala, C.; Corsini, G. U.; Mangoni, A.; Gessa, G. L. Institute of Neurology, University of Cagliari, Cagliari Italy **Effect of apomorphine on human sleep.** Life Sciences. 23(4):403-407, 1978.

The effect of intravenous infusion of apomorphine in nonemetic doses (10-15mcg/minute) on the sleep of 10 human subjects was studied. During apomorphine infusion for 180 minutes, a complete suppression of rapid eye movement (REM) sleep and a dramatic reduction of the amount of delta sleep occurred. Thus, the EEG pattern was characterized almost exclusively by the presence of light sleep. After discontinuation of apomorphine, a rebound increase in REM sleep occurred. These results support the contention that brain catecholamines, particularly dopamine (DA), exert an inhibitory effect on REM sleep and delta phases of sleep in humans. 20 references. (Author abstract)

003621 Cohen, L. no address **A controlled study of Trancopal in sleep disturbances due to rheumatic disease.** Journal of International Medical Research (Northampton). 6(2):111-114, 1978.

A placebo controlled, double-blind study was carried out in six centers in general practice to assess the effectiveness of Trancopal in treating sleep disturbances due to rheumatic disorders. Eighty five patients received a usual dose of two tablets of Trancopal or matching placebo at night for 2 weeks. Patients were assessed weekly and kept a daily record of the quality of sleep. Results indicate that patients slept significantly better on Trancopal than on placebo. Day time rheumatic stiffness however was not significantly reduced. Six patients receiving Trancopal reported side-effects chiefly drowsiness which was controlled by dose reduction. It was concluded that for rheumatic patients Trancopal offers on acceptable alternative to current hypnotics over which it may prove to have some advantages, particularly for the elderly. 4 references. (Author abstract)

003622 DeGood, Douglas E.; Valle, Ronald S. Clinical Psychology Center, 604 Old Engineering Hall, University of Pittsburgh, Pittsburgh, PA 15260 **Self-reported alcohol and nicotine use and the ability to control occipital EEG in a biofeedback situation.** Addictive Behaviors (Oxford). 3(1):13-18, 1978.

Forty college aged males identified as either users or nonusers of alcohol and nicotine underwent four 40 min eyes closed occipital alpha biofeedback sessions over a 4 week period to test the hypothesis that infrequent users of alcohol and nicotine might be better at self-regulation of arousal level, apart from absolute amount of alpha or direction of training. One half of the subjects attempted to enhance their alpha density while the other half attempted to suppress it. Analyses of the alpha control scores indicate that nonusers were superior to users of these substances in the self-regulation of occipital alpha density. The possibility that individuals with poor cortical regulatory ability might be predisposed to use such cortically active substances as alcohol and nicotine is discussed as are several limitations of the present data. 19 references. (Author abstract modified)

003623 DeLiz, Antonio J. District VIII Mental Health - Mental Retardation Center, Marysville, KY 41056 **Interdependence between social processes and neurochemical operations.** Journal of Orthomolecular Psychiatry (Regina) 7(3):167-175, 1978.

A unifying hypothesis, which encompasses the relationships between stressful social relations, central neurochemical processes, and abnormal behavior, is presented. The data on which the hypothesis is based were obtained in field experiments in Appalachia and South East Africa. A complete case history of a 23-year-old Appalachian native who, since he was 10 years old, spent 9 years in jails and reformatories under gruesome conditions. The inference from this man's experiences is that if a disorganized, impoverished, and asocial system may lead to abnormal behavior with serious forms of mental retardation and depression, neurotic or psychotic, and consequent alcoholism, then, conversely, a social system that enhances communication from above downward and vice versa should contribute to information sharing and encourage interaction between individuals and their society. This system shall have the potential for learning and creativity. The theory of the polarity or complementarity of social and neurochemical processes entailed in this study implies that there is some degree of interdependence or mutual dependence, or autonomy, of social and neurochemical factors. Recent data on social stress and the pharmacological action of drugs in animals and humans are presented, and new data on the interdependence of social structure and psychiatric disorders in South East Africa are included. 9 references.

003624 Dries, W. J. H.; Schreurs, W. H. P.; Buyze, G.; Schakelaar, A. J. Psychiatrisch Ziekenhuis Zon en Schild, Amersfoort, The Netherlands **/Study of the influence of vitamin supplements on the behavior of psychiatric patients./** Onderzoek naar de invloed van vitaminesuppletie op het gedrag van psychiatrische patienten. Tijdschrift voor Psychiatrie (Meppel). 20(5):307-314, 1978.

The effects of multiple vitamin administration were studied in 73 hospitalized psychiatric patients who were divided into two equal groups matched in regard to age, sex, diagnosis, and psychiatric treatment. Treatment and medication were kept constant during the experimental period of 3 months. One group received a daily vitamin mixture of B1, B6, B12, C, nicotinamide, and folic acid of two to three times the recommended daily allowance, while the second group received a placebo. Vitamin blood levels were determined before and after the experimental period. The psychiatric effect was assessed by measurement of scores on an egostrength scale and on a social adjustment scale. In several patients subnormal or borderline values for one or more of the vitamin concentrations were found. After supplementation, the concentration of most of the vitamins was significantly increased. Statistical analysis of the scores in the two rating scales used showed an improvement in the vitamin supplemented group, especially in social role behavior and the ability to communicate. It is concluded that it is advisable to supply, as a routine procedure, vitamin supplements to hospitalized psychiatric patients. 25 references. (Journal abstract modified)

003625 Fibiger, H. C. Department of Psychiatry, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada **Drugs and reinforcement mechanisms: a critical review of the catecholamine theory.** Annual Review of Pharmacology and Toxicology. 18:37-56, 1978.

Some of the drug and reinforcement medrauisues and data and arguments upon which the catecholamine (CA) hypothesis rests are examined, and recent experimental results that appear to be incompatible with CA theories are discussed. The CA hypothesis, first proposed by Stein and later elaborated upon by Crow, maintains that the nonadrenaline (NA) axons within the medial forebrain bundle mediate the reinforcing properties of intracranial self-stimulation. Many reports have appeared that point to a correlation between the location of positive self-stimulation sites and the anatomy of ascending NA projections. While it is possible that central NA neurons participate in certain reinforcement processes in a nonessential and nonexclusive manner, there is currently no evidence to support even such a limited role, A better case can be made for an involvement of central dopaminergic neurons in reinforcement. It is concluded that brain stimulation reward is not dependent exclusively upon these dopaminergic systems and that existing noncatecholaminergic systems which can maintain this behavior must be identified. 73 references. (Author abstract modified)

003626 Firestone, Philip; Davey, Jean; Goodman, John T.; Peters, Susan. Children's Hospital of Eastern Ontario, 401 Smyth Road, Ottawa, Ontario K1H 8L1, Canada **The effects of caffeine and methylphenidate on hyperactive children.** Journal of Child Psychiatry. 17(3):445-456, 1978.

The effects of caffeine and methylphenidate on hyperactive children were studied using validated psychological and behavioral assessments. Twenty one hyperactive children received in turn 500mg of caffeine, 300mg of caffeine, and 20mg methylphenidate per day in a double-blind crossover design investigation, and each drug was given for 3 weeks. Methylphenidate resulted in significantly improved behavior in the children as rated by mothers and teachers, and on tests of impulsivity and motor control. There were no significant improvements in either of the caffeine conditions, although some children showed some slight improvements with caffeine. The negative side-effects with both caffeine and methylphenidate were minimal. 46 references. (Author abstract modified)

003627 Fisher, Mary Ann. Dept. of Psychology, University of Maryland Baltimore County, 5401 Wilkens Ave., Baltimore, MD 21228 **Dextroamphetamine and placebo practice effects on selective attention in hyperactive children.** Journal of Abnormal Child Psychology. 6(1):25-32, 1978.

Three groups of three boys referred to a hospital study unit for evaluation of hyperactive behavior were tested on a classification task involving selective attention while on either detroamphetamine (D) or placebo (P). In two sessions, groups had D first, P second (DP), or PD, or PP. Amphetamine is reported to reduce response times in general and to reduce interference due to orthogonally varying irrelevant information. Practice while on placebo improves performance in a subsequent placebo session, however practice while on amphetamine does not improve performance in the subsequent session on placebo. It is concluded that an assessment of the extent of the drug state related practice effect is necessary for evaluation of long-term benefits of dextroamphetamine therapy in hyperactive children. 5 references. (Author abstract)

003628 Gold, Mark S.; Redmond, D. Eugene, Jr.; Kleber, Herbert D. Research Facilities and Substance Abuse Unit, Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT **Clonidine blocks acute opiate-withdrawal symptoms.** Lancet (London). 2(8090):599-602, 1978.

In a double-blind, placebo controlled, cross-over trial, clonidine eliminated objective signs and subjective symptoms of opiate withdrawal for 240-360 minutes in 11 addicts in a hospital setting. In an open pilot study of the effects of clonidine on longer-term opiate abstinence and symptoms, the same patients did well while taking clonidine for 1 week. There was only one documented instance of heroin use, in a patient who did not take clonidine after hospital discharge. Six weeks or more after the study, four patients were back on reduced doses of methadone, one was on tricyclic antidepressants, and seven were off of all opiates. All 11 patients were doing well. Data suggest that opiate withdrawal is due to increased neuronal activity in areas such as the locus coeruleus which are regulated by both alpha-2 adrenergic and opiate receptors. 24 references. (Author abstract)

003629 Hartley, L.; Couper-Smartt, J. Department of Psychology, University of Leicester, University Road, Leicester LE1 7RH, England **Paradoxical effects in sleep and performance of two doses of chlorpromazine.** Psychopharmacology (Berlin). 58(2):201-205, 1978.

This experiment attempted to: 1) confirm the paradoxical effects of low and high doses of chlorpromazine on rapid eye movement (REM) duration and to relate this to the period of the REM/nonREM cycle, and 2) discover if there is a dose related difference in behavior during wakefulness. Twenty four subjects were given placebo, 25 mg, and 75mg of chlorpromazine on three separate occasions. Ss received the drug treatments in the morning or in the evening and had their EEG sleep stages recorded during the subsequent night. The low dose of the drug shortened the rapid eye movement (REM)/ nonREM cycle length in comparison to the high dose. Placebo values were intermediate. In performance tests, visual intergration time was impaired by the high dose of the drug. Logical reasoning was slowed by the high dose of the drug in comparison to the low dose, with placebo values intermediate between the two. 15 references. (Author abstract modified)

003630 Hrbek, J.; Komenda, S.; Macakova, J.; Vinar, O.; Dostalova, K.; Komarkova, A. Dept. of Pathological Physiology, Medical Faculty of the Palacky University, Dr. S. Allende 3, 77515 Olomouc, Czechoslovakia **Acute effects of lisuride (0.1 mg), amantadine (100 mg) and trihexyphenidyl (5 mg) on verbal associations.** Activitas Nervosa Superior (Praha). 20(1):78, 1978.

In a paper read at the 19th Annual Psychopharmacological Meeting, held in Jesenik, Czechoslovakia during January 1977, the acute effects of lisuride, amantadine, and trihexyphenidyl on verbal associations are described. Two hours after drug administration, a significant impairment in number of correct responses and marked impairment in frequency of responses and the number of necessary repetitions were produced by trihexyphenidyl. This effect was most obvious when the artificially conditioned speech connections were established by means of the applied acoustic and complex tactile stimuli. A significant decrease in heartrate was also observed following administration of trihexyphenidyl. 1 reference

003631 Jarvik, Murray E.; Popek, Paulene; Schneider, Nina G.; Baer Weiss, Vivian; Gritz, Ellen R. Veterans Administration Hospital Brentwood, Los Angeles, CA **Can cigarette size and nicotine content influence smoking and puffing rates?** Psychopharmacology (Berlin). 58(3):303-306, 1978.

The effect of nicotine content and cigarette size on smoking and puffing rates was investigated. Nine volunteers, given their own cigarettes in whole, half, quarter, and eighth lengths, increased the number of cigarettes smoked and the number of puffs to compensate for reductions in size. Satisfaction was directly related to cigarette length. In the second experiment, subjects given cigarettes delivering 0.2or 2.0mg nicotine/cigarette smoked significantly more of the low than of the high nicotine cigarettes and took significantly more puffs. Significantly more

quarter length than whole cigarettes were smoked, but total number of puffs did not differ. Results support the hypothesis that nicotine controls smoking behavior. 10 references. (Author abstract modified)

003632 Kramp, P.; Rafaelsen, O. J. Dept. of Psychiatry, Rigshospitalet, 9, Blegdamsvej, DK-2100 Copenhagen 0, Denmark **Delirium tremens: a double-blind comparison of diazepam and barbital treatment.** Acta Psychiatrica Scandinavica (Kobenhavn). 58(2):174-190, 1978.

The effects of diazepam (D) and barbital (B) in the treatment of delirium tremens (DTs) and other acute conditions related to alcohol abuse were compared in a double-blind trial. Ninety one patients participated in the study, 44 in the D group, 47 in the B group. D was chose rather than chlordiazepoxide because of its major anticonvulsive properties. B was given orally, D i.m. A discussion of the routes of administration of drugs to DT patients concluded that the different routes used in the study probably did not affect outcomes. A considerable number of the Ss had D, but not B, in the blood before treatment was initiated. The patients were divided into three diagnostic categories according to the severity of the clinical condition. No difference between the two drugs was found in the milder conditions, but B was superior to D in the treatment of fully developed DTs. 47 references. (Author abstract modified)

003633 Krogh, C.; McLean, W. M.; LaPierre, Y. D. Ottawa General Hospital, 43 Bruyere St., Ottawa, Ont. K1N 5C8, Canada **Minor tranquillizers in somatic disorders.** Canadian Medical Association Journal (Ottawa). 118(9):1097, 1100-1102, 1107-1108, 1978.

A review of the literature shows that conclusive evidence of improved outcome due to adjunctive anxiolytic therapy (minor tranquillizers) in some somatic conditions is lacking. However, such therapy may facilitate patient management without being curative. The resulting improved feeling of well-being may be of value in the management of gastrointestinal disorders, migraine, and myocardial infarction. Negative effects may be observed in acute respiratory conditions, especially during acute exacerbations of chronic conditions, with the administration of benzodiazepines; hence they should be used with caution. The use of these agents in treating persons with hypertension seems to be of no value and may even be detrimental. Careful evaluation of each case is desirable and treatment should be planned with its termination in mind. 55 references. (Author abstract)

003634 Middleton, R. S. W. Dept. of Geriatric Medicine, St. James' University Hospital, Leeds 9, England **Temazepam (Euhypnos) and chlormethiazole: a comparative study in geriatric patients.** Journal of International Medical Research (Northampton). 6(2):121-125, 1978.

The sleep inducing properties and tolerance of temazepam were compared with chlormethiazole syrup in two groups of geriatric in patients. The temazepam was administered as a solution in soft gelatine capsules. Both compounds appeared to be safe, effective and well tolerated, but significant differences in favor of temazepam were observed in quality and duration of sleep, ease of awakening and carry over effects. It is concluded that this formulation of temazepam would appear to be an ideal sleep inducer for geriatric patients. 11 references. (Author abstract modified)

003635 Rundell, O. H.; Williams, Harold L.; Lester, Boyd K. Dept. of Psychiatry and Behavioral Sciences, University of Oklahoma Health Sciences Ctr., P. O. Box 26901, Oklahoma City, OK 73190 **Secobarbital and information processing.** Perceptual and Motor Skills. 46(3, Part 2):1255-1264, 1978.

The Sternberg fixed set memory search paradigm was used to assess the relative vulnerability of hypothetical stages of information processing to an oral dose of 2.9mg/kg secobarbital. D-amphetamine (15mg, oral dose) was intended to serve as an active placebo. However, because the amphetamine produced a slight reduction in reaction time (RT), the principal analysis of secobarbital effects was conducted between drug and baseline conditions. Secobarbital slowed RT by 60 msec and did not increase errors significantly. The results, as interpreted within Sternberg's model, suggest that input processes, e.g.,stimulus preprocessing encoding, are particularly sensitive to the effects of the barbiturate. There was no evidence of a drug effect on cognitive processes associated with serial comparison, binary decision, or translation response organization (response selection). In contrast, earlier studies have indicated that another central depressant, alcohol, interferes with both speed and accuracy of output processes. 16 references. (Author abstract)

003636 Singhal, Radhey L.; Rastogi, Ram B. Department of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada **Neurotransmitter mechanisms during mental illness induced by alterations in thyroid function.** Advances in Pharmacology and Chemotherapy. 15:203-262, 1978.

The influence of variations in thyroid hormone levels on the metabolism of brain norepinephrine, dopamine, 5-hydroxytryptamine, and acetylcholine is examined based on studies in the literature. Evidence for neuroendocrine abnormalities in mental dysfunction, hyperthyroidism and related mental illness, the effect of lithium on behavior and brain monoamines in neonatally hyperthyroid rats, the influence of diazepam on locomotor performance and brain biogenic amines in hyperthyroid rats, similarities between depression and hypothyroidism, neurochemical correlates of suppressed behavior during hypothyroidism, thyroid hormones and the critical period of brain development, and the combined use of tricyclic antidepressants and thyroid hormone are the major topics discussed. The importance of investigating the effects of a psychotropic drug in an experimental model analogous to psychiatric illness for which the drug is employed therapeutically, rather than in normal animals, is stressed. 254 references.

003637 Soldatos, Costas R.; Kales, Anthony; Bixler, Edward O.; Scharf, Martin B.; Kales, Joyce D. Sleep Research and Treatment Center, Milton S. Hershey Medical Center, Hershey, PA 17033 **Hypnotic effectiveness of sodium salicylamide with short-term use: sleep laboratory studies.** Pharmacology (Basel). 16(4):193-198, 1978.

Sodium salicylamide in doses of 650mg and 1300mg was evaluated in two separate laboratory drug evaluation studies of insomniac patients, to determine its effectiveness for inducing and maintaining sleep under conditions of short-term drug administration and to evaluate its effect at each dose on sleep stages. Each study utilized a standard protocol of 10 consecutive laboratory nights consisting of four placebo nights for adaptation and baseline, three drug nights for short-term drug administration and three placebo nights for evaluating withdrawal. Neither dose had a clear cut hypnotic effect in inducing or maintaining sleep, nor were sleep stages affected by drug administration or drug withdrawal. Both objective findings and subjective estimates suggest that the 1300mg dose may have a slight sedative effect, however, when salicylamide is used as an ingredient in over the counter preparations, the usual dose is only 200mg to 400mg. 17 references. (Author abstract modified)

003638 Sunshine, Abraham; Zighelboim, Itic; Laska, Eugene. New York University Medical Center, New York, NY **Hypnotic activity of diphenhydramine, methapyrilene, and placebo.** Journal of Clinical Pharmacology. 18(8-9):425-431, 1978.

In a double-blind controlled study, an oral dose of diphenhydramine hydrochloride (12.5, 25, or 50mg), methapyrilene fumarate (36, 72, or 144mg), or placebo was administered to 1295 postpartum patients who complained of or anticipated sleeping problems. Hypnotic activity was assessed clinically by subjective and objective techniques. Methapyrilene and diphenhydramine, at all doses, were found to be effective hypnotics in comparison to placebo based on sleep latency and duration, awakening, global evaluation, and morning alertness. Increasing the dose of these drugs, in the range studied, produced a minimal increase in effectiveness. 11 references. (Author abstract)

003639 Watson, Stanley J.; Berger, Philip A.; Akil, Huda; Mills, Mark J.; Barchas, Jack D. Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **Effects of naloxone on schizophrenia: reduction in hallucinations in a subpopulation of subjects.** Science. 201(4350):73-76, 1978.

Eleven carefully screened schizophrenic subjects were given high doses of naloxone (10mg) and the reduction or blockade of their auditory hallucinations was observed. The subjects were selected on the basis of the following criteria: they exhibited a stable symptom pattern, had very frequent auditory hallucinations (at least twice per hour), and had an active ratable pathology on the rating scales. Approximately 1000 general psychiatric patients were screened to locate the 11 patients studied. A double-blind, crossover design was used, and the data show that naloxone produced decreases in auditory hallucinations in some schizophrenic patients. This finding supports the hypothesis that the endorphins may play a role in modulating hallucinations in a highly selected subgroup of chronically hallucinating schizophrenic patients. 22 references. (Author abstract modified)

003640 Wolraich, Mark; Drummond, Thomas; Salomon, Marion Kerner; O'Brien, Mary Lynn; Sivage, Carol. University Hospital School, University of Iowa, Iowa City, IA 52242 **Effects of methylphenidate alone and in combination with behavior modification procedures on the behavior and academic performance of hyperactive children.** Journal of Abnormal Child Psychology. 6(1):149-161, 1978.

Twenty hyperactive 6-year-old to 9-year-old children of normal intelligence were studied in a half day laboratory classroom in a two week period baseline treatment reversal design for behavior modification. Under double-blind conditions half the children were placed on .3mg/kg of Ritalin and half on placebo for the entire program. The classroom program consisted of a group period with immediate reinforcement possible, and an individual time period without immediate reinforement possible. Behavior modification caused a significant decrease in nonattending, out of seat, inappropriate vocalizing and inappropriate peer interaction behavior in the group period. Fidgeting, a nontargeted behavior, was not significantly decreased during this period but did significantly decrease as a result of medication. No other drug effects occurred during this period. During the individual period, the results were essentially reversed. There were no sifnificant behavior modification effects observed. Significant reductions resulted from medication in all behaviors except out of seat and fidgeting. Behavior modification alone significantly affected the two academic measures. It is concluded that no significant interactions is noted between medication and behavior modification. 20 references. (Author abstract modified)

003641 Yaryura-Tobias, J. A.; Neziroglu, F. Division of Research, North Nassau Mental Health Center, 1691 Northern Boulevard, Manhasset, NY 11030 **Compulsions, aggression, and self-mutilation: a hypothalmic disorder?** Journal of Orthomolecular Psychiatry (Regina). 7(2):114-117, 1978.

Twelve patients presenting aggressive behavior, obsessive compulsive symptoms, self-mutilation, sexual disorders, insomnia, and disturbances in the family constellation are described. Secondary findiugs in some patients include high pain threshold, abnormal electrocardiogram, and altered glucose tolerance curves. Nine had a past history of anorexia nervosa, and four patients had a history of psychosis. Out of eight treated cases, chlorimipramine, a potent serotonin reuptake blocker, relieved symptoms in 6 patients and worsened them in 2 cases with a history of psychosis. A hypothalmic dysfunction related to a serotonergic imbalance is offered as a hypothesis of work. 13 references. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

003642 Albertini, Ralph S.; Penders, Thomas M. Dartmouth Medical School, Dept. of Psychiatry, Hanover, NH 03755 **Agranulocytosis associated with tricyclics.** Journal of Clinical Psychiatry. 39(5):483-485, 1978.

A case report of agranulocytosis associated with imipramine use is presented, and literature suggesting that this is a rare but hazardous complication of tricyclic use is cited. A possible pathogenesis for this syndrome is suggested, and characteristic findings and treatment are discussed. Agranulocytosis associated with tricyclic use appears to be a rare, idiosyncratic condition resulting from a direct toxic effect rather than an allergic mechanism, and it affects the elderly in particular from 4 to 8 weeks after commencement of treatment. 17 references.

003643 Bailey, David N.; Van Dyke, Craig; Langou, Rene A.; Jatlow, Peter I. Division of Clinical Pathology, University of California Medical Center, 225 West Dickinson St., San Diego, CA 92103 **Tricyclic antidepressants: plasma levels and clinical findings in overdose.** American Journal of Psychiatry. 135(11):1325-1328, 1978.

Results of a Study on tricyclic antidepressant plasma levels in 30 overdose cases are discussed. Following amitriptyline or imipramine overdose, total plasma concentrations ranged from 29 to 1732 ng/ml but did not correlate well with physical findings or most electrocardiographic changes. Only those patients with a QRS interval greater than 0.1sec. had significantly elevated plasma levels. However, a plasma level ratio of the parent drug (amitriptyline, imipramine) to its respective N-desmethyl metabolite (nortriptyline, desmethylimipramine) greater than or equal to 2.0was associated with an acute overdose. This ratio was more useful than total plasma levels in differentiating an overdose from a therapeutic dose with associated toxicity and an elevated steady state plasma level. 24 references. (Author abstract)

003644 Buchanan, Darrell S. Director of Medical Education. Walter Reed Army Medical Center, Washington, DC 20012 **Iatrogenic causes of neurologic disorders: part 2. drug-related dysfunctions.** Geriatrics. 33(9):47-52, 1978.

Drug related disorders involving the motor, sensory, autonomic, and periopheral nervous systems are considered. Motor system disorders tha may result from antipsychotic drugs sometimes respond well to anticholinergics or sedatives but the tardive dyskinesias may persist so that long-term antipsychotic drug therapy in older patients may not be worth the risk of complications. Phenothiazine and streptomycin are known to effect sight and hearing. Nitrofurantoin is identified as the number one cause of drug related peripheral neuropathy in elderly patients. Restraint in the use of drug therapy for older patients is recommended. 5 references.

003645 Burrows, Graham D.; Vohra, Jitu; Dumovic, Pete; Scoggins, Bruce A.; Davies, Brian. Dept. of Psychiatry, Clinical Sciences Building, Royal Melbourne Hospital, Victoria 3050,

Australia **Cardiological effects of nomifensine, a new antidepressant.** Medical Journal of Australia (Glebe). 1(6):341-343, 1978.

A cardiovascular study of a new antidepressant, nomifensine, revealed no significant cardiac effects in eight ambulant patients who received up to 200mg of nomifensine per day for 3 weeks. In an electrophysiological study of cardiac conduction, nomifensine had significantly less effect on cardiac activity than amitriptyline and doxepin. Results of the clinical and the experimental studies suggest that nomifensine may be of value in treating the depressed patient with heart disease. 28 references. (Author abstract)

003646 Chouinard, Guy; Jones, Barry D.; Annable, Lawrence. Research Dept., Hospital Louis-H. Lafontaine, 7401 Rue Hochelaga, Montreal, Quebec Canada HIN 3M5 **Neuroleptic-induced supersensitivity psychosis.** American Journal of Psychiatry. 135(11):1409-1410, 1978.

Neuroleptic-induced supersensitivity psychosis was observed, and the hypothesis that tardive dyskinesia and supersensitivity psychosis may be caused by a similar mechanism occurring in different areas of the brain is proposed. The hypothesis is supported by the common factors that can alter the clinical picture of both syndromes: increasing the neuroleptic dosage decreases the severity of dyskinesia and psychosis, decreasing the dosage makes both worse, stress exacerbates both dyskinetic and psychotic symptoms, and L-dopa and amphetamine can increase the severity of both. The suggestion that neuroleptics can produce a dopamine supersenitivity that leads to both dyskinetic and psychotic symptoms implies that this supersensitivity is irreversible. It is concluded that in some cases, the need for continued neuroleptic treatment may itself be drug induced. 10 references.

003647 Cordoba, Oscar A.; Chapel, James L. no address **Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) secondary to antipsychotic drug therapy.** Missouri Medicine. 75(4):177-178, 181, 1978.

A case study of a patient suffering from the Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH) is presented. A 24-year-old female was admitted to the Medicine Service with symptoms of disorientation, confusion, gradual increase in thirst and polyuria. One month prior to admission she received fluphenazine enanthate. Clinical and laboratory examinations suggested SIADH. The SIADH has been described in psychiatry in association with certain psychoses as well as secondary to psychotropic medication. It is concluded that diagnostic osmolality studies are necessary for the diagnosis and adequate treatment of SIADH cases. 8 references.

003648 Corsini, G. U.; Del Zompo, M.; Spissu, A.; Mangoni, A.; Gessa, G. L. Institute for Nervous and Mental Diseases, University of Cagliari, Cagliari Italy **Parkinsonism by haloperidol and piribedil.** Psychopharmacology (Berlin). 59(2):139-141, 1978.

Three groups of schizophrenic patients were treated with haloperidol, a low dose of the dopamine (DA) agonist piribedil, or a combination of the two drugs. After a few days, all seven patients treated with the drug combination showed marked rigidity and akinesia, while the four patients treated with haloperidol alone and the four patients treated with piribedil alone showed mild or no symptoms of parkinsonism. The drug combination induced mainly an akinetic/hypertonic syndrome, with mild or no tremors. Results suggest that low doses of the DA agonist potentiate the extrapyramidal side-effects of haloperidol by acting on self-inhibitory DA receptors, thereby blocking the compensatory increase in dopaminergic firing elicited by the neuroleptic agent. 11 references. (Author abstract)

003649 Curry, Stephen H. London Hospital Medical College, Turner Street, London E1 2AD, England **Pharmacokinetics and psychotropic drugs.** Psychological Medicine (London). 8(2):177-180, 1978.

The problems associated with bringing psychotropic drugs under pharmacokinetic control by changing their plasma levels are discussed. Some of the problems facing researchers include: the lack of reliable analytic methods, inadequate knowledge of chemistry by lab workers, inaccurate fluid measurements, and the lack of checking centrifugation conditions to determine the presence of hemolysis or cell contamination. It is noted that pharmacokinetic studies are the most effective way to study the pharmacokinetic phenomena of absorption and elimination, and to obtain data on bioavailability and drug interactions. However, major problems still exist in the proper categorization of metabolites. Clinical observations between plasma levels and the use of chlorpromazine and tricyclic antidepressants are discussed. Some rules for clinical relationships are also identified, which appear to be the basis for the difference of opinion among those investigating tricyclic antidepressants. It is concluded that clinical monitoring is useful, and that drug treatment can be more effectively controlled if pharmacokinetic variability is compensated with individually tailored dosage regimens. 18 references.

003650 Deniker, P.; Eyquem, A.; Bernheim, R.; Loo, H.; Delarue, P. Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, Hopital Sainte-Anne, 1, rue Cabanis, F-75674 Paris Cedex 14, France **Thyroid autoantibody levels during lithium therapy.** Neuropsychobiology (Basel). 4(5):270-275, 1978.

The levels of thyroid antibodies were studied in 58 patients treated with lithium and 40 control subjects who received other psychotropic drugs and who were used as controls. Of the 58 patients treated with lithium, 24 were manic-depressives and the others were schizophrenics or patients with mood disorders. Antithyroglobulin antibodies were measured by passive hemagglutination and antimicrosomal antibodies were measured by indirect immunofluorescence. For the control group, the antithyroglobulin antibody research was positive in three cases (7.5%). For the 58 patients treated with lithium, the research was positive in 11 subjects (19%). Five lithium treated patients developed a goiter. The antibody determination was positive in only two subjects and was negative in the others. The measure of antithyroid antibodies before lithium did not predict the emergence of thyroid complications. Results show that subjects treated with lithium presented significantly high antibody levels without developing clinical thyroid manifestations. 15 references. (Author abstract modified)

003651 Donovan, B. T. Department of Physiology, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF **The behavioural actions of the hypothalamic peptides: a review.** Psychological Medicine (London). 8(2):305-316, 1978.

The various activities of the hypothalamic peptides are reviewed and assessed, along with available clinical information. Some of the observed behavioral actions are: 1) vasopressin, ACTH, and like peptides influence memory processes; 2) ACTH and MSH given intracranially induce a peculiar stretching and yawning syndrome accompanied by penile erection and ejaculation, 3) THR potentiates behavioral excitation; 4) somatostatin is depressive; 5) LH-RH facilitates sexual behavior; and 6) the newly identified endorphins are markedly opioid in character. It is concluded that the hypothalamic peptides are gradually usurping the prominent position occupied by the monoamines, and increased knowledge of the peptides' functions will be of great psychiatric significance. 71 references. (Author abstract modified)

003652 Elsworth, J. D.; Glover, Vivette; Reynolds, G. P.; Sandler, M.; Lees, A. J.; Phuapradit, P.; Shaw, K. M.; Stern, G. M.; Kumar, Parveen. no address **Deprenyl administration in man: a selective monoamine oxidase B inhibitor without the 'cheese effect.'** Psychopharmacology (Berlin). 57(1):33-38, 1978.

The pressor effects of (-)-deprenyl, a selective monoamine oxidase B inhibitor, were investigated in four normal and six parkinsonian volunteers. After pretreatment with deprenyl, the Ss suffered no adverse pressor reaction ("cheese effect") when challenged with oral tyramine in amounts considerably greater than those likely to be encountered in a normal diet. No pressor response was observed in the four parkinsonian Ss receiving both levadopa and deprenyl. Similarly, oral phenylethlamine challenge in amounts greater than those known to be present in a normal diet gave rise to no adverse reaction in deprenyl treated Ss. 29 references. (Author abstract modified)

003653 Evans, Larry. University of Queensland, Dept. of Psychiatry, Clinical Sciences Bldg., Royal Brisbane Hospital, Brisbane, Queensland, Australia 4029 **A case of lithium poisoning? A cautionary tale.** Australian and New Zealand Journal of Psychiatry (Rozelle). 12(2):133-135, 1978.

In a paper presented at the 14th Annual Congress of the Royal Australian and New Zealand College of Psychiatrists in Brisbane, October 1977, the case of a 58-year-old woman on maintenance lithium therapy who developed an acute organic brain syndrome is reported. The patient subsequently shoed evidence of persistent brain-damage. It is suggested that lithium toxicity was precipitated by electrolyte disturbances possibly caused by self-medication with a diuretic; this caused serum levels of lithium to be an unreliable measure of impending toxicity. 17 references. (Author abstract modified)

003654 Flaherty, Joseph A.; Lahmeyer, Henry W. Dept. of Psychiatry, Abraham Lincoln School of Medicine, University of Illinois, 912 South Wood St., Chicago, IL 60680 **Laryngeal-pharyngeal dystonia as a possible cause of asphyxia with haloperidol treatment.** American Journal of Psychiatry. 135(11):1414-1415, 1978.

Two case reports of patients with respiratory distress associated with the use of the nonphenothiazine antipsychotic haloperidol whose symptoms were relieved by diphenhydramine are described, and the relationship between these cases and published reports of phenothiazine related sudden deaths is discussed. It is hypothesized that these patients were suffering from a laryngeal/pharyngeal dystonia induced by haloperidol. The objective signs in these cases seem to rule out the possiblity of simple panic attacks with hyperventilation, although a component of this seems likely. 10 references.

003655 Gardos, George; Cole, Jonathan O.; Tarsy, Daniel. Institute for Research and Rehabilitation, Boston State Hospital, 591 Morton St., Boston, MA 02124 **Withdrawal syndromes associated with antipsychotic drugs.** American Journal of Psychiatry. 135(11):1321-1324, 1978.

Withdrawal syndromes associated with antipsychotic drugs are described and discussed. In addition to other somatic symptoms, withdrawal emergent dyskinesias may be observed. Covert dyskinesia refers to a masked form of tardive dyskinesia that becomes clinically detectable only after antipsychotic drugs are withdrawn or their dosage is reduced. Withdrawal dyskinesia appears under similar circumstances but disappears spontaneously, usually in 6 to 12 weeks. Cholinergic overactivity and changes in dopamine/acetylcholine balance in the basal ganglia may underlie these withdrawal syndromes. The principal value of the concept of covert dyskinesia is in the secondary and tertiary prevention of tardive dyskinesia through early discovery and treatment. 39 references. (Author abstract)

003656 Gerlach, J.; Simmelsgaard, H. Sct. Hans Hospital, Dept. H, DK-4000 Roskilde, Denmark **Tardive dyskinesia during and following treatment with haloperidol, haloperidol biperiden, thioridazine, and clozapine.** Psychopharmacology (Berlin). 59(2):105-112, 1978.

In a crossover trial, i6 elderly psychiatric patients with tardive dyskinesia (TD) were treated with thioridazine (median dose, 267.5mg/day) for 3 months, followed by haloperiodol (5.25mg/day), haloperidol plus biperiden (6mg/day), thioridazine, and clozapine (62.5mg/day) for periods of 4 weeks, with 4 week drug free intervals. At the end of the treatment periods, the hyperkinesia score for haloperiodol treatment was lower than that for thioridazine or haloperidol plus biperiden treatment periods. Clozapine had no significant antihyperkinetic effect, but exerted a clear antiparkinsonian effect in one patient. Biperiden increased the TD syndrome during treatment but did not significantly influence the syndrome after withdrawal of the treatment. It is concluded that haloperidol has a more pronounced antihyperkinetic effect than thioridazine and clozapine and may have a greater tendency to induce TD. Administration of anticholinergics concomitant with neuroleptic drugs appears to antagonize the antihyperkinetic effect of haloperidol but may not influence the intensity of TD after withdrawal of the treatment. 38 references. (Author abstract modified)

003657 Hindmarch, I.; Parrott, A. C. Department. of Psychology, University of Leeds, Leeds LS 2 9JT, England **A repeated dose comparison of the side effects of five antihistamines on objective assessments of psychomotor performance, central nervous system arousal and subjective appraisals of sleep and early morning behaviour.** Arzneimittel-Forschung (Aulendorf). 28(3):483-486, 1978.

The side-effects of five antihistamines (chlorpheniramine maleate; mebhydrolin; clemastine hydrogen fumarate, Tavegil; ketotifen; and promethazine hydrochloride) were measured on subjective assessments of sleep and the integrity of early morning behavior and objective assessments of complex psychomotor behavior and central nervous system arousal. fucifty consenting volunteers each received one of the five preparations for a period of 4 days with the subjective effects being reported on a set of 10 cm line visual analogue scales and the objective assessments being made via a computer assisted reaction task and critical flicker fusion thresholds. Chlorpheniramine produces a significant impairment in critical flicker fusion thresholds with respect to pretreatment baselines but none of the preparations showed any significant impairment in complex reaction time assessments. The subjective assessments of sleep and early morning hangover showed mebhydrolin and clemastine to be free from detrimental side-effects, but promethazine and chlorpheniramine produced significant impairments in the iegrity of early morning behavior. 10 references. (Author abstract modified)

003658 Hollender, Marc H.; Jamieson, Robert C.; McKee, Embry A.; Roback, Howard B. Dept. of Psychiatry, School of Medicine, Vanderbilt University, Nashville, TN 37232 **Anticholinergic delirium in a case of Munchausen syndrome.** American Journal of Psychiatry. 135(11):1407-1409, 1978.

A case report of self-induced anticholinergic delirium in a case of Munchausen syndrome is described. In recent years various atropine-like postsynaptic blockers have been substituted for atropine sulfate in the practice of ophthalmology. Also, since other anticholinergic medications may be used systemically, producing an additive effect, it is more appropriate to speak of anticholinergic delirium than the term atropine delirium. To

differentiate pupillary change produced by eye drops from neurologic disease, pilocarpine, a parasympathomimetic agent, is safe and reliable. The patient was found to have ingested chlorpromazine, amitriptyline, scopolamine, and tropicamide. 10 references.

003659 Kennedy, L. A.; Persaud, T. V. N. Teratology Research Laboratory, Dept. of Anatomy, University of Manitoba, Winnipeg, Manitoba R3E OW3, Canada **Pentobarbital intoxication in the pregnant rat.** Research Communications in Chemical Pathology and Pharmacology. 20(1):179-182, 1978.

Pentobarbital intoxication was examined in pregnant Sprague-Dawley rats who were treated intraperitoneally with low doses of pentobarbital, 5, 15, or 25mg/kg, on days 9 through 12 of gestation. Results indicate no significant differences in fetal weight, length, or placental weight. Other than minor ossification delays, there were no external, skeletal or visceral abnormalities and no treatment related variation in fetal mortality. Microscopic examination of various maternal and fetal tissues revealed no major deleterious effects of short-term pentobarbital intoxication. 5 references. (Author abstract modified)

003660 Levinson, Peritz; Malen, Richard; Hogben, George; Smith, Harry. 120 East 89th St., New York, NY 10028 **Psychological factors in susceptibility to drug-induced extrapyramidal symptoms.** American Journal of Psychiatry. 135(11):1375-1376, 1978.

In an effort to identify nonneurobiologic factors in the susceptibility to neuroleptic-induced extrapyramidal symptoms (EPS), the EPS response in 20 patients was correlated with field dependence, self-object differentiation, and premorbid social competence. Premorbid social status was found to correlate with EPS unsusceptibility. However, the fact that field dependence and self-object differentiation did not correlate with EPS responses weakens the support for psychological causality and suggests that premorbid adjustment consists of diverse dimensions. 18 references. (Author abstract modified)

003661 Levy, Norman B. Box 127, Downstate Medical Center, 450 Clarkson Ave., Brooklyn, NY 11203 **Psychological sequelae to hemodialysis.** Psychosomatics. 19(6):329-331, 1978.

The psychological complications of hemodialysis treatment are described, suggesting that psychological complications occur as a response to the unusual stresses imposed by the dependency and inconvenience of the procedure. Depression, suicidal behavior, uncooperativeness, and sexual incapacity are identified as the major effects of hemodialysis. Counseling is recommended prior to commencement of hemodialysis in order to inform patients of possible side effects, such as 70% chance of impotence in males. While psychotropic medication may have a role in the treatment of hemodialysis complications, most psychoactive medications are unusable because they are excreted by the kidneys. Lithium and the major tranquilizers are cited as exceptions to this prohibition. It is concluded that the psychologically attuned professional can play a major therapeutic role that may notably improve the quality of life for hemodialysis patients. 17 references.

003662 Lobo, Antonio; Pilek, Eugene; Stokes, Peter E. Departamento de Psiquiatria y Psicologia Medica, Hospital Clinico Universitario, Planta 11, Zaragoza, Spain **Papilledema following therapeutic dosages of lithium carbonate.** Journal of Nervous and Mental Disease. 166(7):526-529, 1978.

A possible hazard of therapeutic dosages of lithium carbonate in a patient with circular manic-depressive illness is presented. The 29-year-old female patient had received therapeutic dosages of lithium carbonate, but developed papilledema that seemed to be directly related to the drug. Although this is an extremely rare complication, it is suggested that fundal examinations may be considered in patients treated with lithium. 11 references. (Author abstract modified)

003663 Luchins, Daniel J.; Sherwood, Paul M.; Gillin, J. Christian; Mendelson, Wallace B.; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, Intramural Research Program, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Filicide during psychotropic-induced somnambulism: a case report.** American Journal of Psychiatry. 135(11):1404-1405, 1978.

A case report of a 44-year-old woman who stabbed her daughter to death during psychotropic drug-induced somnambulism is described. Subsequent research in a sleep laboratory revealed that the woman walked in her sleep following combinations of thioridazine and chloral hydrate. The mechanism by which psychotropic drugs induce sleepwalking remains obscure. It is possible that they interfere with an inhibitory system which normally prevents somnambulism. It is cautioned that administration of large bedtime doses or various psychotropics in those with a history of sleepwalking (and, perhaps, other stage 4 abnormalities) should be avoided. 9 references.

003664 Lullmann, Heinz; Lullmann-Rauch, Renate; Wassermann, Otmar. Department of Pharmacology, University of Kiel, Kiel, Germany **Lipidosis induced by amphiphilic cationic drugs.** Biochemical Pharmacology (Oxford). 27(8):1103-1108, 1978.

Lipidosis induced by amphiphilic cationic drugs, including antidepressants, neuroleptics, and other psychotropic drugs, is discussed. Drug-induced lipidosis can be viewed as a drug side-effect or as a cytological phenomenon which might be a useful tool in cell biology. The therapeutic risk of applying a lipidosis inducing drug should be balanced against the risk of the disease. While drug-induced lipidosis may prove useful for studying the cytological events of lysosomal storage of endogenous material, it is not an appropriate experimental model for studying inherited human lipidosis. Drug-induced lipidosis is a fairly unspecific alteration of substrates rather than an inhibition or reduction of a particular enzyme that leads to intralysosomal accumulation of polar lipids. 66 references.

003665 Mann, John; Branton, Lesley J.; Larkins, Richard G. Neuropsychopharmacology Research Unit, NYU Medical Center, 550 1st Ave., New York, NY 10016 **Hyperosmolality complicating recovery from ilithium toxicity.** British Medical Journal (London). 1(6126):1522-1523, 1978.

Two case reports are presented of patients with a history of polydipsia and polyuria associated with lithium therapy who developed delirium and hyperosmolality while recovering from lithium toxicty. The accepted regimen for management of lithium toxicity is intravenous saline. It is asserted that 12% of patients taking lithium develop a syndrome involving inability to concentrate urine in the presence of a continuing salt load, and can thus develop hyperosmolality. The importance of monitoring osmolality in such patients during treatment of lithium toxicity is emphasized. 5 references.

003666 McAfee, Heidi Ann. Allentown College of St. Francis de Sales, Department of Nursing, Center Valley, PA 18034 **Tardive dyskinesia.** American Journal of Nursing. 78(3):395-397, 1978.

The clinical features, pathophysiology, and treatment of tardive dyskinesia, a side-effect of long-term phenothiazine administration, are discussed. Tardive dyskinesia appears relatively late after initiation of drug therapy and is characterized by athetoid or choreiform movements, which are rhythmic and coordinated. Most often the movements involve sucking and smacking

movements of the lips, lateral jaw movements, and projection of the tongue. The pathogenesis of the syndrome is explained by the receptor blockade theory. Drugs that partially alleviate symptoms include haloperidol (Haldol), thiopropazate (Dartal), reserpine (Serpasil), physostigmine (Antilirium), and deanol (Deaner). 12 references.

003667 McGennis, A. J. St. John's Day Centre, Clontarf, Dublin 3, Ireland **Lithium carbonate and tetracycline interaction.** British Medical Journal (London). 6121:1183, 1978.

A case report of a potentially serious interaction between lithium carbonate and tetracycline is presented. The administration of tetracycline to a female manic-depressive patient caused an increased concentration of serum lithium which resulted in drowsiness, tremor, and slurred speech. It is concluded that: 1) the physician should always be on his guard when lithium is combined with any medication that may affect renal function; and 2) the case illustrates the value of routine serum lithium measurement. 4 references.

003668 Moskovitz, Charlene; Moses, Hamilton, III; Klawans, Harold L. Institute for Psychosomatic and Psychiatric Research and Training, Michael Reese Hospital and Medical Center, Chicago., IL **Levodopa-induced psychosis: a kindling phenomenon.** American Journal of Psychiatry. 135(6):669-675, 1978.

The prevalence of three types of psychiatric side-effects of antiparkinsonian drug therapy, especially levodopa, which can generate as well as reactivate hallucinations and psychoses, was investigated. Vivid dreams, hallucinatory experiences, and psychotic thought disorders were examined retrospectively and cross-sectionally in 88 patients with idiopathic Parkinson's disease. Although the subjects had no prior psychotic symptoms and no significant dementia, nearly half had experienced the psychiatric side-effects of chronic levodopa therapy. The findings suggest that chronic levodopa therapy may result in dopaminergic kindling and support the hypothesis that chronic dopaminergic agonism may, through such a kindling mechanism, play a role in the development of some types of psychoses. 51 references. (Author abstract modified)

003669 Neil, John F.; Merikangas, James R.; Davies Robert K.; Himmelhoch, Jonathan M. Assessment and Brief Treatment Unit, Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburg, PA 15261 **Validity and clinical utility of neuroleptic-facilitated electroencephalography in psychotic patients.** Clinical Electroencephalography. 9(1):38-48, 1978.

Electroencephalographs (EEGs) of 83 schizophrenics who had been hospitalized for evaluation of suspected medical/neurological disorder were studied to evaluate the validity, utility, and intraindividual consistency of neuroleptic associated EEG patterns in psychotic patients. Patients were studied before and during treatment with therapeutic oral doses of neuroleptic medications. Patients displaying paroxysmal epileptiform abnormalities only after antipsychotic drug treatment did not differ significantly from those displaying these patterns during both drug free and posttreatment conditions. Both groups displayed significantly greater evidence of episodic oneiroid features and preexisting minimal brain dysfunction than did patients with normal pretreatment and posttreatment EEGS. A high degree of intraindividual consistency of EEG drug responsiveness was observed in patients studied during consecutive trials of two or more chemically distinct neuroleptic compounds. It is suggested that neuroleptic mediated activation of paroxysmal dysrhythmias occurs more frequently in susceptible individuals with an electrophysiologic predisposition toward this pattern. 36 references.

003670 Nininger, James E. Department of Psychiatry, Cornell University School of Medicine, New York, NY **Inhibition of ejaculation by amitryptyline.** American Journal of Psychiatry. 135(6):750-751, 1978.

A case report of complete failure to ejaculate during orgasm while under treatment for depression with amitriptyline is reported. The side-effect ceased within one day of stopping the medication, after four months of treatment with the drug. Possible causes of this side-effect are discussed. It is suggested that ejaculatory failure is underreported due to embarrassment, and that a discussion of possible ejaculatory side-effects with patients would be beneficial. 7 references.

003671 no author. no address **Preventing drug-induced dyskinesia.** Medical World News. 19(3):76-77, 1978.

At the December meeting of the American College of Neuropsychopharmacology held in San Juan, Puerto Rico, the problem of detection, prevention and possible treatment of drug-induced tardive dyskinesis was examined by numerous experts. Tardive dyskinesia (TD) is a late appearing lingering motor disorder which has been identified as a side-effect of such neuroleptic compounds as the phenothiazines. TD is precipitating not only the specter of malpractice suits but reappraisal of antipsychotic drug therapy. Antipsychotic drugs blockade dopamine receptor sites in the striatal nigral area of the extrapyramidal nucleus. With persistent blockade, receptors increase at postsynaptic sites, and any passage of dopamine across the synapse to overstimulate the receptors triggers the dyskinetic response. With the termination of therapy, the receptor sites are unoccupied by drug molecules, and the TD effect worsens. The risk of TD is difficult to estimate and conflicting reports have been presented. It is suggested that monitoring patients, occasionally diverting treatment programs, and a newly developed overloading technique may effective in heading off the disorder.

003672 Nutt, J. G.; Neophytides, A. N.; Lodish, J. R. National Institutes of Health, Bethesda, MD 20014 **Lowered erythrocyte-sedimentation rate with sodium valproate.** Lancet (London). 2(8090):636, 1978.

Indirect evidence that may corroborate the report of Dale et al.,that sodium valproate can cause depletion of fibrinogen is presented. The erythrocyte-sedimentation rate (ESR) was monitored in 19 adult patients who received sodium valproate in doses of 2-3g per day for 3-5 weeks as an experimental therapy for various movement disorders. The ESRs before and after valproate treatment did not differ significantly. The ESRs during high dose treatment were significantly lower than the before and after treatment values. Fibrinogen measurements on and off valproate were obtained during the study in three patients; fibrinogen decreased during therapy, but values remained within normal limits. If the lowering of the ESR does reflect reduction of plasma fibrinogen by sodium valproate, the effect may be more prevalent than a single case report suggests. Findings emphasize the recommendation of Dale et al. that coagulation be monitored during long-term therapy with the drug. 2 references.

003673 Okada, Fumihiko; Kase, Manabu; Shintomi, Yoshiko. Health Administration Center, Hokkaido University School of Medicine, Sapporo, Japan. **Pupillary abnormalities in schizophrenic patients during long-term administration of psychotropic drugs: dissociation between light and near vision reactions.** Psychopharmacology (Berlin). 58(3):235-240, 1978.

Pupillographic studies were made of the reactions to light and near vision of 12 schizophrenic patients under long-term administration of psychotropic drugs. Results showed a significant reduction in the light reaction, while the near vision reaction was preserved. The pupillographic study revealed not only reduc-

tion in amplitude of the light reaction, but also changes in dynamic aspects of the reaction, such as prolonged latency time, shortened constriction time, and half redilatation time after the light stimulus. The mechanisms underlying the dissociation between light reaction and near vision reaction induced by long-term administration of psychotropic drugs are obscure, but both peripheral and central actions of these drugs may be involved. 12 references. (Author abstract)

003674 Overall, John E. Department of Psychiatry, University of Texas Medical Branch, Galveston, TX 77550 **Prior psychiatric treatment and the development of breast cancer.** Archives of General Psychiatry. 35(7):898-899, 1978.

The possible implications for the development of breast cancer due to increased prolactin levels that result from treatment with major neuroleptic drugs was investigated. A search of the computerized records of a large university hospital was made to identify all women from 1967 to 1976 whose conditions had been diagnosed as breast cancer or primary cancer of another site. The records for those women with diagnoses of cancer were then examined to identify any prior psychiatric diagnoses. The rationale was that most patients treated in this hospital setting for psychiatric disorders received neuroleptic drugs, and patients with a diagnosis of schizophrenia are almost certain to be treated with major neuroleptic drugs over a prolonged period of time. No substantial difference in the relative frequency of prior psychiatric treatment was observed between breast cancer and other cancer groups. Data support the conclusion that increased risk of breast cancer, due to psychiatric drug treatment, is not a clinically substantial problem where schizophrenia is the alternative. 12 references.

003675 Petho, Bertalan; Tariska, Peter; Pinter, Katalin; Sommer, Edy. Psychiatrische Universitatsklinik, Balassa u. 6, H-1083 Budapest VIII, Hungary **/On the role of hemispheric dominance in schizophrenia as measured by extrapyramidal side-effects of neuroleptics./** Uber die Rolle der haemispharielien Dominanz bei Schizophrenien, gemessen an den extrapyramidalen Begleiterscheinungen der Neuroleptika. Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 30(1):23-27, 1978.

Phenomena observed during treatment of schizophrenic patients with neuroleptics were measured clinically in an attempt to determine the difference in vulnerability of the two hemispheres and the relation between this difference and schizophrenic diseases. In the group of systematic schizophrenias, the increase in tonus was significantly higher in the dominant hemisphere. This finding is considered a verification of the nosological hypothesis of schizophrenia. 11 references. (Journal abstract)

003676 Raskind, Murray A.; Kitchell, Margaret; Alvarez, Carrol. Geriatric Research, Education and Clinical Center, Seattle Veterans Administration Hospital, 4435 Beacon Ave. S., Seattle, WA 98108 **Bromide intoxication in the elderly.** Journal of the American Geriatrics Society. 26(5):222-224, 1978.

Case histories of four elderly patients with a dysfunction of the central nervous system secondary to bromide intoxication are reported. Three of them were referred because of senility symptoms, which appeared to preclude further independent living. After diagnosis and treatment of the bromism, they were able to continue living at home. The development of bromide toxicity with relatively low serum bromide levels in the elderly is discussed. The importance of a home visit to establish the diagnosis of drug-induced cognitive dysfunction is emphasized. 10 references. (Author abstract)

003677 Reisberg, Barry. Neuropsychopharmacology Research Unit, PQ3, Dept. of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Single case study. Catatonia associated with disulfiram therapy.** Journal of Nervous and Mental Disease. 166(8):607-609, 1978.

A catatonic syndrome occurring in a patient receiving disulfiram treatment is reported. A causal relationship is strongly suggested by the mode of onset, the absence of a previous history of catatonia, and the rapid resolution of the syndrome within 72 hours of discontinuance of the disulfiram therapy. Neurophysiological mechanisms which aid in elucidating the role of disulfiram in the etiology of catatonia are discussed. It is important that physicians be alerted to this serious complication, as it is readily reversible if the disulfiram is discontinued and appropriate supportive measures are taken. Also, it appears that these patients may be more susceptible to complications with future disulfiram usage. 10 references. (Author abstract modified)

003678 Sheehy, L. Michael; Maxmen, Jerrold S. Dept. of Psychiatry, Columbia University College of Physicians and Surgeons, New York, NY 10032 **Phenelzine-induced psychosis.** American Journal of Psychiatry. 135(11):1422-1423, 1978.

A case report of a patient who seemed to have had a phenelzine-induced psychosis that did not resemble the usual, albeit infrequently reported, behavioral side effects of monoamine oxidase inhibitors, is presented. Although the cause of the patient's brief psychosis cannot be determined with certainty, it appeared to be either a direct phenelzine-induced side-effect or a drug-triggered psychosis in a highly vulnerable patient. Because the psychosis occurred when full clinical response to phenelzine would first be expected and resolved promptly after it was discontinued, it is concluded that the phenelzine was the offending agent. 4 references.

003679 Siegal, Frederick P. Memorial Sloan-Kettering Cancer Center, New York, NY 10021 **Lithium for steroid-induced psychosis.** New England Journal of Medicine. 299(3):155-156, 1978.

In a letter to the editor, a case study is reported in which lithium carbonate mitigated the mental changes associated with corticosteroids (prednisone) in a patient being treated for nonHodgkin lymphoma. The steroid induced psychosis and limited further treatment until lithium therapy was instituted. It was then possible to reinstitute prednisone treatment. It is concluded that if lithium can be used to minimize or eliminate steroid-induced psychosis, the indications for lithium will be widened, and the applicability of steroids improved.

003680 Simpson, George M.; Varga, Ervin; Lee, J. Hillary; Zoubok, Boris. University of Southern California, Department of Psychiatry, 1934 Hospital Place, Los Angeles, CA 90033 **Tardive dyskinesia and psychotropic drug history.** Psychopharmacology (Berlin). 58(2):117-124, 1978.

The adult population of a large mental hospital was screened for tardive dyskinesia (TD) to investigate the role of neuroleptic intake and organic factors in the development of TD. Approximately 11% of the patients showed signs of TD; females and the elderly were overrepresented in the TD group. A representative sample of those with TD was selected and matched with control patients for age, sex, length of hospitalization, diagnosis, and race. The charts of these subjects were examined for any indices of brain damage, and the complete psychotropic drug history was recorded. There was no difference in the TD and non-TD groups in the amount of psychotropics ingested, duration of administration, kinds of drugs, or organicity history. Women as a group tended to have more polypharmacy than men. The role of neuroleptics and other possible etiological factors in TD are discussed. 24 references. (Author abstract)

003681 Smith, James M.; Oswald, William T.; Kucharski, L. Thomas; Waterman, Laura J. Office of Clinical Research,

Harlem Valley Psychiatric Center, Station A, Wingdale, NY 12594 **Tardive dyskinesia: age and sex differences in hospitalized schizophrenics.** Psychopharmacology (Berlin). 58(2):207-211, 1978.

An examination of the severity of tardive dyskinesia in 293 hospitalized schizophrenics using the Abnormal Involuntary Movement Scale revealed differing trends with age for each sex. Females showed a significant linear increase in severity with age, while males had a significant curvilinear relationship. Reliable differences between sexes were found only for patients aged 70 and older. The differences in sexes could not be accounted for by differences in length of current hospitalization or current level of neuroleptic medication. Possible reasons for the results are discussed. 20 references. (Author abstract modified)

003682 Smith, Robert C.; Strizich, Michael; Klass, David. Lab. of Behavioral Neurochemistry, Texas Research Institute of Mental Sciences 1300 Moursund, Texas Medical Center, Houston, TX 77030 **Drug history and tardive dyskinesia.** American Journal of Psychiatry. 135(11):1402-1403, 1978.

In a study of drug history and tardive dyskinesia in chronically hospitalized mental patients, drug histories of 103 older patients were examined to determine the correlation between drug and dosage variables and scores on the Smith Tardive Dyskinesia Scale. Analysis reveals that only one drug, fluphenazine, consistently had small to moderate positive correlations with tardive dyskinesia scores. Intramuscular injections of fluphenazine enanthate correlated closely with the development of facial dyskinesia. Contrary to expectations, tardive dyskinesia was significantly negatively related to the total amount of neuroleptics that a patient had received. 10 references.

003683 Sovner, Robert; DiMascio, Albert; Berkowitz, David; Randolph, Peter. 591 Morton Street, Boston, MA 02124 **Tardive dyskinesia and informed consent.** Psychosomatics. 19(3):172-173, 176-177, 1978.

The thesis is presented that the time has come to reappraise the need for written informed consent when neuroleptic drugs are prescribed because of the risk that patients will develop tardive dyskinesia (TD). This extrapyramidal syndrome alters the risk/benefit ratio of neuroleptic drug therapy for two distinct groups of patients: those who receive neuroleptic agents continuously for more than one year, and those who already have TD but must nevertheless continue treatment with these agents. Written informed consent for treatment should be obtained from these two groups of patients as a condition for neuroleptic drug therapy to protect both patients and clinicians. Evidence is presented that such written consent will not adversely affect patient compliance. 31 references. (Author abstract modified)

003684 Summerfield, Arthur. Department of Psychology, Birkbeck College, University of London, London, England /**Behavioral toxicity: the psychology of drug pollution.**/ Behavioural toxicity -- the psychology of pollution. Journal of Biosocial Science (Cambridge). 10(3):335-345, 1978.

The concept of behavioral toxicity (adverse psychological effects of chemicals absorbed into the body) is discussed historically and traced from its recent origins in psychopharmacology. The concept became a significant issue in connection with the new "psychotropic" drugs of the 1950s and has remained so. Changes in behavior can be among the most sensitive indicators of toxic effects. Investigations of behavioral toxicity are considered together with their implications for further improvement of behavioral methods for the early detection of toxic effects of pollutants. Chemical pollution caused by industrial accidents, chemical additives in food, and airborne pollutants are discussed. 47 references. (Author abstract modified)

003685 White, Kerrin. Los Angeles County-University of Southern California Medical Center, 1934 Hospital Place, Los Angeles, CA 90033 **Tricyclic overdose in a patient given combined tricylic-MAOI treatment.** American Journal of Psychiatry. 135(11):1411-1412, 1978.

A case report of a tricyclic overdose in a patient given combined tricylic/MAOI treatment is described, and the hypothesis that such combination therapy poses special risks to patients who ovedose is discussed. This patient, after more than a month of combined tricyclic/MAOI treatment intentionally overdosed on the tricyclic and presented a clinical picture consistent with typical tricyclic overdose. No hypertension, hyperthermia, or seizures occurred. This observation contrasts with the few catastrophic case reports of similar overdose situations, which have contributed to the bias against such combination therapy. 9 references.

003686 Zahavi, J.; Schwartz, G. Thrombosis Research Unit, King's College Hospital Medical School, London SE5 8RX, England **Chlorpromazine and platelet function.** Lancet (London). 2(8081):164, 1978.

Small doses of chlorpromazine were found to cause significant prolongation of bleeding time in apparently health individuals but caused no change in in-vitro platelet function tests. This conclusion supports the proposition that drugs like chlorpromazine, which stabilize red cell membranes, may represent a novel approach to the prevention of arterial thrombosis. The findings also seem to support Born's explanation that an increase in bleeding time is caused by a decrease in the hemostatic efficacy of the platelets through an action of chlorpromazine on the red blood cells, possibly by diminishing the leakage of adenosine diphosphate from them. 12 references.

003687 Zavodnick, Steven. 411 S. 11th St., Philadelphia, PA 19147 **A pharmacological and theoretical comparison of high and low potency neuroleptics.** Journal of Clinical Psychiatry. 39(4):332-336, 1978.

The side-effects of high and low potency neuroleptics are compared. Low-potency drugs are more likely to cause central, autonomic and peripheral side-effects of all types with the exception of extrapyramidal symptoms. The tendency to produce tardive dyskinesia cannot be compared as relevant data do not currently exist. Greater affinity for the dopamine receptor and 20 to 70 fold greater milligram and molar potency are advanced as arguments for greater specificity of high potency drugs in the treatment of psychoses. It is proposed that the high potency neuroleptics might be considered the drugs of choice in the treatment of schizophrenia and schizophreniform psychoses. 31 references. (Author abstract)

16 METHODS DEVELOPMENT

003688 Burger, D.; Lairy, G. C. Laboratoire de Neurophysiologie Clinique et de Psychophysiologie. Experimentale. Hopital Henri, Rousselle, Paris, France. **Multivariate analysis of drug-effects on electrophysiological signals in man.** Neuropharmacology (Oxford). 17(11):891-904, 1978.

A multidimensional analysis method (Prinipal Component Analysis) for the study of drug effects on electrophysiological signals, such as the electroencephalogram and electrocardiogram, is described. The method provides a mapping of the data which permits formulation of hypotheses on their structure as well as elaboration of a statistical processing strategy. The method also permits detection and correction of parasite effects that may distort or conceal the drug effect itself. 8 references. (Author abstract modified)

003689 Filip, Vaclav; Balik, Josef. Psychiatric Research Unit, Medical School of Charles University, Ke Karlovu 11, 128 21 Prague 2, Czechosolvakia **Possible indication of dopaminergic blockade in man by electroretinography.** International Pharmacopsychiatry (Basel). 13(3):151-156, 1978.

Dopaminergic blockade was demonstrated by means of electroretinography (ERG). The effect of 50mg thioridazine was compared with that of placebo in two groups of 10 normal volunteers. In the placebo group, the postdrug scotopic ERG was not significantly different from the predrug ERG; while in the thioridazine group, the postdrug scotopic ERG showed prolongation of "a" wave latency time, prolongation of "b" wave evolution time, and diminution of "b" wave amplitude. These findings are consistent with the expected consequences of drug-induced dopaminergic blockade. Further research into the possible use of the ERG in evaluation of psychotropic drugs is recommended. 4 references. (Author abstract modified)

003690 Forrest, I. S.; Green, D. E.; Serra, M. T.; Chao, F. C.; Loeffler, K. O. Biochemical Research Laboratory, V. A. Hospital, Palo Alto, CA 94304 **Chlorpromazine excretion. II. Improved TLC procedures for fractionating the urinary drug content into chemical subgroups of CPZ metabolites.** Communications in Psychopharmacology. 2(2):131-138, 1978.

The development of improved thin layer chromatography (TLC) procedures for fractionating unconjugated chlorpromazine (CPZ) metabolites in solvent extracts from whole urine or aglycones from the hydrolyzed conjugated derivatives, is described. Although these multistep procedures are cumbersome and time consuming, they produce subfractions containing manageable numbers of compounds, thereby facilitating one dimensional or two dimensional TLC gas chromatography or gas chromatography/mass spectrometry analyses. Since attempts are being made in various hospitals and laboratories to correlate clinical data with patterns of drug metabolism, or the presence, absence, or relative abundance of a specific metabolite, separation procedures facilitating the fractionation into such subgroups of metabolites, as e.g. sulfoxides and hydroxylated compounds, are useful. 5 references. (Author abstract modified)

003691 Jimerson, David C.; Gordon, Edna K.; Post, Robert M.; Goodwin, Frederick K. Biological Psychiatry Branch, NIMH, Bethesda, MD 20014 **Homovanillic acid in human CSF: comparison of fluorimetry and gas chromatography-mass spectrometry.** Communications in Psychopharmacology. 2(4):343-349, 1978.

Homovanillic acid (HVA) levels in 64 samples of lumbar cerebrospinal fluid (CSF) from psychiatric patents were determined by fluorimetric assay and by a gas chromatographic/mass spectrometric (GC-MS) method. Direct comparison of HVA determinations by these two methods reveal a high interassay correlation in both baseline and higher, postprobenecid ranges. Fluorimetric values were consistently lower than those obtained by GC-MS. It is concluded that fluorimetric assay of VA in human CSF is internally consistent and suitably reliable, particularly in the higher ranges seen after probenecid treatment. 21 references. (Author abstract modified)

003692 Kallman, M. J.; Rosecrans, J. A.; Chance, W. T. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Drug discrimination paradigms: problems of tolerance and behavioral disruption.** Psychopharmacology (Berlin). 58(2):7, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, the use of drug discrimination paradigms in evaluating the development of drug tolerance and cross-tolerance to nontrained drug cues was discussed. Data from investigations on the stimulus properties of nicotine and morphine were presented to show how measures of tolerance and behavioral disruption can be obtained from rates of schedule performance, how selection of reinforcement parameters can enhance the behavioral disruption observed, and how testing procedures can affect measures of generalization and behavioral disruption. (Author abstract modified)

003693 Lapierre, Y. D. Psychopharmacology Unit, Ottawa General Hospital, 197 Cumberland, Ottawa, Ontario K1N 7H4, Canada **Assessment of long-acting neuroleptics. Methods and problems.** International Pharmacopsychiatry (Basel). 13(3):157-164, 1978.

Methodological considerations in the preclinical and clinical assessment of long lasting neuroleptics drugs are discussed. These drugs, without offering a therapeutic breakthrough in the treatment of schizophrenia, are nevertheless a definite step in the management of patients with this disorder. The adequate assessment of these agents necessitates methodological considerations to ensure adequate patient selection, adaptations to the drugs' characteristics, sufficient duration of the study, and special precautions in the assessment of toxicity. Furthermore, patient management in such studies must assure continued and easy accessibility of both the investigating and the treating team. 12 references. (Author abstract modified)

003694 Sjoquist, Birgitta; Johansson, Barbro. Department of Pharmacology, Karolinska Institutet, S-104 01 Stockholm 60, Sweden **A comparison between fluorometric and mass fragmentographic determinations of homovanillic acid and 5-hydroxyindoleacetic acid in human cerebrospinal fluid.** Journal of Neurochemistry (Oxford). 31(3):621-625, 1978.

Homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) in human cerebrospinal fluid were quantitatively determined by fluorometry and by mass fragmentography. The HVA values obstained by fluorometry were significantly lower than those obtained by mass fragmentography. The correlation coefficient between values for HVA obtained by the two methods was high (0.90). For 5-HIAA, the concentrations obtained by the two methods were not significantly different but the correlation was lower (0.55). 19 references. (Author abstract)

17MISCELLANEOUS

17 MISCELLANEOUS

003695 Appel, J. B.; White, F. J.; Kuhn, D. M. Behavioral Pharmacology Laboratory, Department of Psychology, University of South Carolina, Columbia, SC 29208 **The use of drugs as discriminative stimuli in behavioral pharmacodynamics.** Psychopharmacology (Berlin). 58(2):3, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, studies on the relationship between lysergic acid diethylamide (LSD), quipazine, anticholinergic hallucinogens, and the serotonergic (5-HT) neuronal system were reported. Findings indicate that the discriminative stimulus properties of LSD and quipazine are identical and similar to those of other 5-HT agonists. These properties partially mimic the discriminative stimulus properties of anticholinergics. They are blocked by 5-HT but not by dopamine antagonists and are not affected by manipulations that alter the reuptake of 5-HT. Results indicate that postsynaptic 5-HT or, possibly, hallucinogen receptors mediate the discriminative properties of both LSD and quipazine. (Author abstract modified)

003696 Arthur, Glenys P. Neurology Department, Wellington Hospital, Private Bag, Wellington 2, New Zealand **Drug treatment of migraine and its variants.** Current Therapeutics (Seaforth, Australia). 19(5):63-64, 67-68, 70, 72, 74, 1978.

Therapeutic procedures for the management of migraine are described. Migraine occurs most frequently in women of reproductive age and consists of an initial phase of cranial vasoconstriction followed by vasodilation. Precipitating factors are enumerated which are believed to cause the release of the vasoconstrictor serotonin in migrainous individuals with a deficiency of monoamine oxidase enzymes. It is recommended that migraine treatment begin with the elimination of aggravating factors and the relief of associated conditions such as hypertension. Suggested treatment of acute attacks ranges from analgesics to varying dosages of ergotamine. For interval and preventive treatment, or for more severe migraine, pizotifen, cyproheptadine, propanolol, pindolol, clonidine, methysergide, or monoamine oxidase inhibitors are recommended.

003697 Attwood, D.; Gibson, J. Pharmacy Department, University of Manchester, Manchester M13 9PL, U.K. **Aggregation of antidepressant drugs in aqueous solution.** Journal of Pharmacy and Pharmacology (London). 30(3):176-180, 1978.

Light scattering, conductivity, and pH methods were used to examine the aggregation in aqueous solution of a series of antidepressant drugs. The drugs investigated include the hydrochlorides of amitriptyline, butriptyline, protriptyline, nortriptyline, imipramine, desipramine, clomipramine, dothiepin, dibenzepin, opipramol, iprindole, doxepin, mianserin, and maprotiline. No significant association of dibenzepin, mianserin, or maprotiline hydrochlorides could be detected up to their respective solubility limits. A micellar pattern of association was established for all other compounds. Critical micelle concentrations and micellar properties are reported. 19 references. (Author abstract)

003698 Baldessarini, Ross J.; Fischer, Josef E. Department of Psychiatry, Harvard Medical School, Boston, MA 02178 **Trace amines and alternative neurotransmitters in the central nervous system.** Biochemical Pharmacology (Oxford). 27(5):621-626, 1978.

Trace amines and alternative neurotransmitters in the central nervous system are reviewed. Trace amines may arise metabolically in association with the synthesis of other amine neurotransmitters and may have regulatory or other physiologically important actions are cotransmitters. Some such substances may even arise independently in unique neurons that do not synthesize the classical transmitters (catecholamines, serotonin, and acetylcholine). Unusual accumulations of trace amines, possibly leading to their acting as substitute or "false" transmitters, may occur in response to a variety of drug treatments and may contribute to the pathophysiology of metabolic, neurological, or psychiatric disorders. 40 references.

003699 Balster, Robert L.; Pross, Roxanne S. Pharmacology Department, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Phencyclidine: A bibliography of biomedical and behavioral research.** Journal of Psychedelic Drugs. 10(1):1-15, 1978.

A 203 item bibliography on phencyclidine (PCP) covering the chemical, biomedical, and behavioral research literature published in the English language in archival sources through early 1978 is presented. The following literature is excluded: articles in the popular press concerning sociocultural studies or the political/legal issues; papers on the use of PCP for restraint of nonhuman primates in veterinary practice where the intent was not to evaluate the effects of PCP; and papers on PCP analogues, unless the research was a direct comparison with PCP. It is noted that PCP has emerged as a recreational drug in the United States and has become a major public health concern. The bibliography is designed to provide a resource for interested individuals to sort fact from fiction about the drug.

003700 Beardsley, Robert Sheldon. University of Minnesota **Evaluation of a patient drug self administration program. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 789627, HC$15. MF$7.50. 208 p. 1977.

The effects of a patient drug self-administration program in a large metropolitan hospital whose main goal was to increase appropriate drug use by patients after they were discharged was evaluated. During the program patients learned about their medications from pharmacists and nurses and practiced taking their medications under hospital staff supervision. Patients gradually assumed more responsibility for administering their medications. Findings show that the program increased both patient compliance and drug knowledge. A significant interaction between treatment group and locus of control revealed that the self-administration program was effective only for those participants who were classified as internal. In addition, it is reported that patients interacting with pharmacists during their hospital stay were more satisfied with pharmacy services and perceived pharmacists as being more knowledgeable about prescription drugs than those patients who did not interact with pharmacists. However, patients rated physicians as their first choice as sources of information about prescription medications and pharmacists as their first choice for nonprescription drug information. (Journal abstract modified)

003701 Becker, Joseph; Schuckit, Marc A. University of Washington, Seattle, WA 98105 **The comparative efficacy of cognitive therapy and pharmacotherapy in the treatment of depressions.** Cognitive Therapy and Research. 2(2):193-197, 1978.

An evaluation of a recent study by Rush et al. (1977) that cognitive therapy is more effective than pharmacotherapy in the treatment of chronically and recurrently depressed patients is

presented. The medication type, dosage level, and duration used by Rush is called into question. It is noted that no single antidepressant drug can provide optimal drug treatment for a broad range of depressives. Furthermore, the durable superiority of cognitive over drug treatment is not consistently supported by Rush's followup data. It is suggested that further research on the efficacy of cognitive behavioral approaches with clinically depressed patients is needed. 24 references.

003702 Breskin, Linda Seltzer. New York University **The effects of appropriateness of attributed arousal source and test anxiety on complex test performance and reported anxiety during test-taking. (Ph.D. dissertation).** Disseration Abstracts International. Ann Arbor, MI, Univ. M-films, No. 78-8450, HC$15. MF$7.50. 178 p. 1977.

In an attempt to learn more about the process of attribution by spelling out the nature of the interaction between levels of physiological arousal and the appropriateness of the externally supplied explanations for this arousal, subjects in a test situation were given the opportunity to reattribute their arousal feelings to an arousal (placebo) pill, the test itself (control), or a relaxation (placebo) pill. The A-State Anxiety scale and the Test Anxiety Scale were used to measure levels of arousal. No interaction was found between level of test anxiety and the appropriateness of the explanation of arousal on complex test performance and on reported anxiety. The failure to achieve the hypothesized results is explained in terms of both methodological and theoretical issues. (Journal abstract modified)

003703 Butler, Robert N. National Institute on Aging, Bethesda, MD **/Heroin and other humanistic treatment for the terminally ill.** "A consummation devoutly to be wish'd." Medical World News. 19(4):88, 1978.

More humane treatment of the terminally ill, including scheduling of analgesic drugs to keep the patient free of pain, use of the most effective analgesics (incluing heroin), counseling the dying, and hospices are discussed. Noting that both the National Institute of Health and the White House have recently shown interest in reforming medical treatment of the terminally ill, the need for objective testing of both marihuana and heroin for use by the terminally ill is emphasized. The hospice is described as a place dedicated to providing comfort, support, and dignity for those who are dying, which should not require construction of new facilities. It is hypothesized that improved scheduling of analgesics will eliminate the specter of fear and pain experienced by the dying.

003704 Capone, Thomas A.; Brahen, Leonard S.; Brahen, Roslyn. Dept. of Graduate Psychology, Hofstora University Hempstead, NY 11550 **Psychoanalytic and behavioral considerations in antagonist and methadone programs.** Journal of Contemporary Psychotherapy. 9(2):139-150, 1978.

Patient/staff dynamics in a narcotic antagonist treatment program are examined and compared to those of conventional methadone therapies. Etiological considerations in addiction are explored from an ego psychology perspective. Psychotherapeutic treatments specific to antagonist programs are contrasted to those of methadone programs. Emphasis is placed upon the integration of antagonist treatment with the patient's developmental phase specific needs. It is asserted that the nonaddictive nature of opiate antagonists promotes self-regulatory ability in the patient. 25 references.

003705 Chouinard, Guy; Jones, Barry D. Research Department, Institute National de la Recherche Scientifique, Hopital Louis-H. Lafontaine, Montreal, Quebec, Canada **Schizophrenia as a dopamine-deficiency disease.** Lancet (London). 2(8080):99-100, 1978.

In a letter to the editor it is hypothesized that schizophrenia is caused by dopamine receptor hypersensitivity resulting from a central dopamine deficiency. Two types of dopamine neurons in the mesolimbic system (comparable to the two types of neurons, dopamine inhibited and dopamine facilitated, possibly found in the striatum) are postulated. It is noted that when firing frequency increases abnormally, the dopamine inhibited neurons would be responsible for the expression of the negative symptoms of schizophrenia, while the facilitated neurons would be responsible for the positive symptoms. Both clinical and pharmacological evidence are given to support this theory. The name tardive psychosis is proposed to describe the association that has been observed between psychotic relapse and tardive dyskinesias after withdrawal of neuroleptics. It is suggested that a more efficient way to treat schizophrenia would be to add levodopa to neuroleptics in patients with signs of dopamine hypersensitivity while, for patients without hypersensitivity (those with only negative symptoms), levodopa alone might prevent and/or reverse the development of dopamine receptor hypersensitivity in addition to treating the negative symptoms. 12 references.

003706 Claridge, Gordon. Department of Experimental Psychology, University of Oxford, South Parks Road, Oxford OX1 3UD, England **Animal models of schizophrenia: the case for LSD-25** Schizophrenia Bulletin. 4(2):186-209, 1978.

The difficulties of trying to establish an animal model of schizophrenia are discussed and the evidence on the experimental psychopathology of schizophrenia, particularly that concerned with attention and arousal, is reviewed. It is suggested that the core feature that needs to be modeled in animals is some aspect of input dysfunction. The use of LSD-25 is recommended because the phenomenology of an LSD model psychosis closely parallels that of the natural disease and because experimental effects of the drug in animals and man are similar to those of schizophrenia. Laboratory research where LSD was found to produce psychological effects identical to those occuring naturally in psychotic personalities is discussed. It is suggested that the rejection of LSD as a drug model is premature. 91 references. (Author abstract modified)

003707 Colpaert, F. C. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Narcotic cue, narcotic analgesia, and the tolerance problem.** Psychopharmacology (Berlin). 58(2):4, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, studies on the possible development of tolerance to the physiological drug effects underlying the narcotic cue were reported. Findings indicate that sensitivity to the narcotic cue does not decrease upon prolonged contingent exposure to a supra effective training dose. Noncontingent exposure before training to doses higher than the training dose increases the discriminability of the narcotic training drug, and noncontingent exposure to such doses does not decrease sensitivity if the exposure is accompanied by contingent exposure to the training dose. Individual sensitivity to the narcotic cue does not covary with susceptibility to narcotic analgesia. It was concluded that tolerance does not develop to the physiological drug actions underlying the narcotic cue and narcotic analgesia. (Author abstract modified)

003708 Cooper, Steven J. Department of Psychology, Queen's University of Belfast, Belfast, Ireland **Psychotropic drugs in pregnancy: morphological and psychological adverse effects on offspring.** Journal of Biosocial Science (Cambridge). 10(3):321-334, 1978.

Evidence on the possible teratogenic risks (adverse morphological and psychological effects produced in the fetus) associat-

ed with taking psychotropic drugs during pregnancy is reviewed, and drug withdrawal syndromes in the newborn are discussed. On the whole, clinically prescribed psychotropic drugs appear to be relatively devoid of serious teratogenic risk. There is some evidence suggesting that a small risk may accompany exposure to certain minor tranquilizers at the early stages of pregnancy. Of those drugs which are commonly taken without prescription by women during pregnancy, narcotics, alcohol, and nicotine can impair fetal development. Narcotic dependency in the newborn and the fetal alcohol syndrome (which includes a constellation of physical abnormalities) are described. 29 references.

003709 Crammer, J. L. Institute of Psychiatry and Maudsley Hospital, London SE5, England **Psychosis in young doctors.** British Medical Journal (London). 1(6112):560-561, 1978.

The case histories of three young doctors who had serious psychotic illnesses as final year medical students are related in order to illustrate how some conditions are fully controllable with psychotropic drugs. Judgment of each individual in terms of what he can do rather than reliance on generalizations about stress or on psychodynamic hypotheses was preferred in these cases. In two of the cases, there were damaging recurrences; however, all three men have subsequently succeeded as clinical practitioners. Since treatment with phenothiazines and support, one doctor has completed five healthy years and the others have completed two years each. (Author abstract modified)

003710 Davis, Kenneth L.; Berger, Philip A.; Hollister, Leo E.; Barchas, Jack D. Veterans Administration Hospital, Palo Alto, CA 94304 **Cholinergic involvement in mental disorders.** Life Sciences. 22(21):1865-1872, 1978.

The recent resurgence of interest in possible cholinergic mechanisms in the pathogenesis of schizophrenia, mania, and depression is discussed. Current research approaches focus more on the interdependent relationships of neurotransmitters than on the actions of the individual transmitters. The treatment of Parkinson's disease, for example, has moved from a cholinergic approach to one that makes important use of dopaminergic mechanisms. It is not yet clear if a reverse shift, from dopaminergic toward cholinergic approaches, is justified in treating schizophrenia. However, persuasive evidence has been adduced to justify cholinergic approaches to the treatment of mania and depression. The development of centrally active cholinomimetic agents will permit the clinical testing of some of the hypotheses engendered by the revival of interest in the role of acetylcholine in emotional disorders. 61 references. (Author abstract modified)

003711 Eich, J. E.; Weingartner, H.; Stillman, R. C.; Wyatt, R. J. Department of Psychology, University of Toronto, Toronto M5S 1A1, Canada **State-dependent retrieval of item, associative, and serial-order information.** Psychopharmacology (Berlin). 58(2):5, 1978.

At the First International Symposium on Drugs as Discriminative Stimuli, held in Beerse, Belgium, July 1978, studies of state dependent retrieval of information in human memory were reported. Specifically, the kinds of memonic information rendered irretrievable as a consequence of a charge of drug state between the acquisition and test sessions of an experiment were examined. Findings suggest that state changes interfere with utilization of information specifying serial order relations among the to be remembered events, but have no appreciable influence on the retrieval of item information or associative information. Implications of these findings for theories of state dependent retrieval and human memory were discussed. (Author abstract modified)

003712 Frey, Douglas D.; Hetherington, Robert W.; Glassman, David. University of Saskatchewan, Saskatoon, Canada **The use of prescription drugs in treatment of first-time psychiatric admissions to University Hospital, Saskatoon.** Social Science & Medicine (Oxford). 12(3A):169-174, 1978.

Patterns of drug administration to first time psychiatric patients were examined. The medical records of a sample of 100 first time admissions to a Canadian university psychiatric ward were investigated. A heavy reliance on drug therapy was found for all periods of care (prehospital, during hospital stay, and posthospital). During hospitalization 3% of the sample received no drugs, while 23% received no psychotherapy; 10% may have received a significant course of psychotherapy. No relationship was found between relative amount of psychotherapy and readmission, but significantly more psychotherapy was provided upon readmission. Minor tranquilizers were more likely to be prescribed for women than for men. Questions are raised about encouraging reliance on licit drugs as a primary coping mechanism for problems in mental health, especially for first admissions and for the relatively youthful population in the study. 10 references. (Author abstract modified)

003713 Graham-Smith. no address **Drug interactions.** London, Macmillan, 1977. L15.00.

An updated series of papers from the British Biological Council Symposium on Drug Interaction held at the Middlesex Hospital in March, 1975 is presented. This is the seventh in a series, five of which deal with various aspects of pharmacology. The volume is divided into five sections, including: 1) general aspects of the problem of drug interactions, 2) mechanisms in drug interactions, 3) drug interactions in psychopharmacology, 4) the influence of diseases on drug effects and interactions, and 5) specific examples of drug interactions.

003714 Gryll, Steven L.; Katahn, Martin. Merriman Hall, Team II, Waterbury Hospital Health Center, Waterbury, CT 06720 **Situational factors contributing to the placebo effect.** Psychopharmacology (Berlin). 57(3):253-261, 1978.

The influence of four variables (status of communicator of drug effects, attitude of dentist, attitude of dental technician, and message of drug effects) on the placebo effect was investigated in an oral surgery clinic. Dependent variables were rating of pain experienced from mandibular block injection, anxiety before and after placebo, and fear of injection before and after placebo. Enthusiastic messages of drug effects produced statistically and clinically significant reductions in postplacebo fear of injection and state anxiety, as well as markedly lower ratings of pain experienced during injection of local anesthetic. Although there was a strong tendency for positive placebo effects to occur when the dental staff was perceived as friendly and supportive, only the attitude factors were statistically significant. The status of the communicator accounted for very small portions of the variance. 42 references. (Author abstract modified)

003715 Iversen, Leslie L.; Iversen, Susan D.; Snyder, Solomon H. Department of Pharmacology, University of Cambridge, Cambridge, England **Handbook of psychopharmacology. Vol. 11. Stimulants.** New York, Plenum Press, 1978. 476 p.

Amphetamines and related stimulants are discussed in terms of the relations between their activity and structure, their central stimulant effects on animals, and their clinical uses. Individual chapters cover the following topics: amphetamine structure/activity relationships; their biochemical and behavioral actions in animals; historical aspects and clinical effects of central nervous system stimulants; drug treatment in child psychiatry; the history of use of plants and plant constituents as mind altering agents throughout the world; the structure/activity relationships

of psychotomimetic drugs; principles of drug metabolism and the fate of one ring psychotomimetics; psychotomimetic drugs in humans; and nicotine addiction and smoking.

003716 Kaumeier, S. Pfalzklinik Landeck, D-6749 Klingenmunster 2, Germany **The pharmacokinetic aspects of therapy with psychotropic agents.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 16(1):27-31, 1978.

In a consideration of the pharmacokinetic aspects of psychotropic agents, the concept that plasma levels of psychotropic agents govern their pharmacodynamic action is appraised. There are at least three problems: identification of the chemical course of reaction between the introduced pharmacon and its resultant metabolites in reference to the totality of the organism and its biochemical reaction pattern; the course of this reaction to intraindividual and interindividual differences; and the influence of the kinetics as a result of concentration diversities, conditioned by different distributing patterns within the organism. Decisive factors here are: mode of application, blood distribution volume, reaction and/or elimination rate, and interaction of combined drugs. 24 references. (Author abstract)

003717 Kline, Neal A. Jewish Family Service, 3355 Fourth Ave., San Diego, CA 92103 **Lithium and crisis intervention: damping affective overload.** Psychosomatics. 19(7):401-405, 1978.

Lithium carbonate's effectiveness as an antidepressant is demonstrated in three case reports. In each, tricyclic antidepressants had been tried unsuccessfully. With lithium's introduction, however, the depressions remitted and suicidal preoccupation which was prominent in each case, diminished rapidly. Damping the affective overload enabled ego reorganization and psychotherapy to proceed. Lithium's rapid action makes it a valuable tool for crisis intervention and suicide prevention. 31 references. (Author abstract)

003718 Leff, David N. no address **Doctors debate brain hormone dilemmas.** Medical World News. 19(1):86-88, 93, 95-96, 1978.

At an international symposium devoted to the use of endorphins in mental health research, the controversy over the use of beta-endorphins on human psychiatric patients is reported along with a discussion of the long-range potential benefits of the drug. The conference was held in San Juan, Puerto Rico in December of 1977 and was sponsored by the National Institute of Mental Health. The report of the use of beta-endorphin on 14 patients suffering from a variety of mental disorders and one control was criticized as observational and anecdotal. Therefore it was hard to justify the use of a compound which had not been tested for toxicity. The development of an enzyme-proof analogue of endorphin which retains 50% of its affinity for opiate receptors is related. The possible relation between schizophrenia and an aberrant enkephalin molecule rather than a mere excess of enkephalin is also discussed. It is concluded that endophrenology may produce at least one important new drug for mental health in the next decade that will operate by a totally new mechanism. (pro-gen)

003719 Lippmann, Steven. Dept. of Psychiatry, University of Louisville, Louisville, KY 40208 **Depression -- a good approach for the non-psychiatrist: III -- how to use the tricyclics.** Resident & Staff Physician. 24(8):111-114, 117, 1978.

Guidelines for the use of tricyclic antidepressants are presented. Dosages, side-effects, contraindications, interactions, and overdose in the treatment of depression with amitriptyline, desipramine, doxepin, imipramine, nortriptylene, and protriptylene are outlined. The importance of warning patients about possible side-effects and lag times for effectiveness is stressed. The need to pay close attention to cardiovascular side-effects in elderly patients is cited. It is recommended that dosage levels be reviewed at each patient visit. Tricyclic maintenance therapy after recovery is discussed. 10 references.

003720 Lisciani, R.; Baldini, A.; de Feo, G.; Silvestrini, B. Silvestrini: Director of Research, Angelini Francesco SpA, Viale Amelia 70, I-00181 Rome, Italy **Pharmacological investigations on etoperidone, a new psychotropic agent.** Arzneimittel-Forschung (Aulendorf). 28(3):417-423, 1978.

The main pharmacological properties are described of 2-(3-(4-(m-chlorophenyl)-1-piperazinyl)propyl)-4,5-diethyl-2, 4-dihydro-3H-1,2,4-triazol-3-one monohydrochloride (etoperidone), a new psychotropic drug which is difficult to classify within the usual classes of psychotropic drugs. Although etoperidone has sedative properties, it differs from the minor tranquilizers in some fundamental aspects, that is, in its interaction with the main cerebral amines, in its lack of anticonvulsant effects, and in its different spectrum of behavioral effects at high doses. Etoperidone also differs from the tricyclic antidepressants in that it does not antagonize resperpine in the rat nor does it potentiate l-dopa behavioral effects in the mouse; moreover, it inhibits the peripheral effects of norepinephrine (NE) and serotonin (5-HT). Etoperidone, however, is similar in some aspects to the neuroleptics such as chlorpromazine, since it produces analgesic, deconditioning and sedative effects at low doses; unlike the neuroleptics, however, it does not block central dopaminergic receptors, as indicated by the absence of catatonia and antagonism of l-dopa and amphetamine in grouped mice. Etoperidone differs from the above mentioned drugs on account of its capacity to selectively inhibit the response of animals to unpleasant stimuli at doses which do not produce other pharmacological effects. The possible clinical uses of etoperidone are discussed. 26 references. (Author abstract modified)

003721 Little, J. C.; Kerr, T. A.; McClelland, H. A. Department of Clinical Research, Crichton Royal, Dumfries, Scotland **Where are the untreated depressives?** British Medical Journal (London). 1(6127):1593-1594, 1978.

Reasons for a shortage of untreated depressives available for clinical trials of antidepressant drugs are examined. A reduction in referrals with depressive disorders is attributed to the increasing use of antidepressants by general practitioners and to a reduction of rereferrals of recurrent manic-depressive psychoses owing to the increasing use of lithium in secondary prevention. It is concluded that henceforth psychiatrists can pursue drug trials in depressive illness only under two conditions: in collaborative multicenter investigations; and by utilization of the depressive patient population of general practitioners. 5 references.

003722 O'Connell, Kathleen Ann. University of Kansas. **Factors influencing willingness to comply and actual compliance with medication regimens. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 789372, HC$15. MF$7.50. 168 p. 1977.

To measure the effects of severity of illness, perceived discomfort of illness, and perceived results of regimen on willingness to comply and on actual compliance with medication regimens, 102 adults who were under prescribed medication regimens for the treatment of medical conditions were presented with 18 hypothetical situations which systematically varied the variables. Participants were asked to indicate how likely they would be to comply with a standard medication regimen if each of the situations were true. Medications that made patients feel better were significantly more likely to induce willingness to comply than medications that made the patients feel no different or worse. In addition, it was found that patients were more will-

ing to comply in situations that were severe and in which the medicine would reduce the severity than in situations that were minor or situations that were severe but in which the medication would not reduce the severity. (Journal abstract modified)

003723 Odejide, A. O.; Ayinde, O. Department of Psychiatry, University College Hospital, Ibadan, Nigeria **Psychotropic and antiparkinsonian drug use: an examination of prescription practices.** African Journal of Psychiatry (Lagos). 4(1,2):31-36, 1978.

The prescription pattern of neuroleptic and antiparkinsonian drugs in the University College Hospital, Ibadan, Nigeria, is described. Multiple dose regime is found to be the practice at admission and also during the maintenance phase. Antiparkinsonian drugs are prophylactically used, while hypnosedatives are also commonly prescribed. The practice of a single daily dose regime is advocated since this reduces the cost of management, interferes less with the intellectual and physical ability of the recepients during the daytime, lessens feelings of dependence, and considerably reduces the use of antiparkinsonian and hyponosedative drugs. It is concluded that the single daily dose regime of neurolepties is adventageous in the maintenance treatment of psychotic illness. 21 references. (Author abstract)

003724 Pihl, R. O.; Shea, Diane; Caron, Paul. McGill University, Montreal, Quebec, Canada **The effect of marihuana intoxication on blood pressure.** Journal of Clinical Psychology. 34(2):569-570, 1978.

Changes in blood pressure in experienced marihuana smokers under two dosage levels and a placebo and coltsfoot, condition were studied. Forty eight experienced marihuana smokers were assigned to one of four groups: coltsfoot, placebo, low dose marihuana and high dose marihuana. While both marihuana groups showed significant increases in subjective ratings of intoxication and pulse rate, blood pressure readings were unaffected or showed a modest decrease. This latter finding is discrepant with previous studies and is explained in terms of a drug X person interaction present in those studies. 4 references. (Author abstract modified)

003725 Prastka, George J. 440 Fair Drive, Costa Mesa, CA 92626 **Neurotransmitter theory and orthomolecular practice.** Journal of Orthomolecular Psychiatry (Regina). 7(2):86-93, 1978.

Chemical therapy for mental illness and its relation to the current knowledge of neurotransmitter theory is reviewed along with the biogenic amine hypothesis of distorted perceptions in schizophrenia. Diet, vitamins, and minerals used in more dramatic ways and dosages than usual may favorably alter various levels of neurotransmitters. Despite task force reports rejecting the efficacy of megavitamin therapy, these therapies persist because experience has shown them to work. It is noted that headaches have never been proven to be due to a deficiency of aspirin in the body, nor depression to be a deficiency of chlorpromazine. It is concluded that although the orthomolecular psychiatrist tries to provide the optimum environment for the mind and brain in as natural a manner as possible: replacing what is needed and removing what is harmful; he is not adverse, as some critics have implied, to using any technique which can bring about favorable results. 39 references.

003726 Rush, A. John; Hollon, Steven D.; Beck, Aaron T.; Kovacs, Maria. University of Oklahoma, Norman, OK 73069 **Depression: must pharmacotherapy fail for cognitive therapy to succeed?** Cognitive Therapy and Research. 2(2):199-206, 1978.

In response to a critique by Becker and Schuckit (1978), the authors defend their comparison study of cognitive therapy with imipramine hydrocholoride on outpatients with chronic and recurrent depressions. The comparative value of cognitive therapy may exist for chronically depressed patients, but may not extend to less chronic populations. It is noted that in the experiment, the pharmacotherapy reflected the best clinical practice available at the time. It is emphasized that the study was designed to answer the question of whether or not cognitive therapy would exceed the efficacy of the usual clinically available treatment either in the reduction of symptoms of the depressive syndrome or in prophylaxis. 5 references.

003727 Shear, M. Katherine; Sacks, Michael. Cornell University Medical School, 525 East 68th Street, New York, NY 10021 **Digitalis delirium: psychiatric considerations.** International Journal of Psychiatry in Medicine. 8(4):371-381, 1978.

Case reports of two patients presenting with psychiatric symptomatology, later identified as digitalis delirium, are given; and psychiatric considerations in digitoxicity are discussed. Digitoxicity is one of the more common iatrogenic disorders. Psychiatric problems, often overlooked as manisfestations of digitalis excess, may range from mild disorientation and lethargy to delirium characterized by hallucinations, irritability, delusional thoughts, mood lability, and severe disorientation. Psychiatrists are advised to consider digitalis as a possible cause of mental abnormalities and are reminded that psychiatric signs may be the first indication of potentially lethal drug toxicity. Psychiatric patients may also be at special risk for digitoxicity because of erratic drug taking, electrolyte imbalance, or increased autonomic tone. 24 references. (Author abstract modified)

003728 Snyder, Solomon H. Department of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD 21218 **Neuroleptic drugs and neurotransmitter receptors.** Journal of Continuing Education in Psychiatry. 39(9):21-31, 1978.

Studies of the dopamine receptors which have enhanced our understanding of the therapeutic actions of neuroleptic drugs are reviewed, and it is shown that the evidence that these agents exert their therapeutic actions by blocking dopamine receptors is as strong as the evidence for the mechanism of action of almost any drugs in clinical medicine. The effects of neuroleptic drugs on muscarine cholinergic and alpha-noradrenergic receptors can predict the relative propensities of the drugs to elicit extrapyramidal and sedative hypotensive side-effects, respectively. Tardive dyskinesia has been shown to be related to an augmentation in the number of dopamine receptors, which may elicit behavioral supersensitivity. Finally, dopamine receptor binding has provided an approach to a simple and specific radioreceptor assay for neuroleptics which may enhance the therapy of schizophrenic patients. Neurotransmitters are the body chemicals which account for therapeutic effects of medications and possibly for disease states as well. The understanding of the interaction of psychotropic drugs with neurotransmitters, particularly with receptor sites, has clarified the actions of drugs in psychiatry. 31 references.

003729 Touyz, S. W.; Beumont, P. J. V.; Saayman, G. S.; Stern, D. A.; Zabow, T. Department of Psychology, University of Cape Town, Rondebosch, South Africa **Placebo and sleep patterns of normal young adults.** Biological Psychiatry. 13(4):481-484, 1978.

The effect of placebo administration on 14 young adults; 7 subjects, 7 controls, with a mean age of 21.20 was examined using multiple indices. A nine consecutive night, double-blind, cross-over design was used. EEGs and electrooculograms were monitored continously throughout the night with the data being analyzed using a two way analysis of variance with repeated measures. Results compared to the control group indicate that the placebo had no significant effect upon any of the sleep indices. It is concluded that the administration of the placebo as a

sleeping tablet has no significant effect upon a multiplicity of sleep parameters in a group of 7 normal young adults. 10 references.

003730 Verebey, Karl; Volavka, Jan; Clouet, Doris. Testing and Research Laboratory, New York State Office of Drug Abuse Services, 80 Hanson Place, Brooklyn, NY 11217 **Endorphins in psychiatry: an overview and a hypothesis.** Archives of General Psychiatry. 35(7):877-888, 1978.

An overview of the biochemistry, pharmacology, and physiology of endogenous opioid peptides (endorphins) is presented. Clinical psychopharmacology of exogenous opiate agonists and antagonists is reviewed. The evidence presented is compatible with a hypothesis that the level of functional endorphins may be related to psychological events, with a normal level needed for psychological homeostasis. One corollary of this hypothesis is that the level of opioids in the brains of the mentally ill may be disturbed. Therapeutic implications of this hypothesis are considered. 188 references. (Author abstract)

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